This transcript is the uncertified transcript of the California DHS Human Stem Cell Research (HSCR) Advisory Committee meeting held on February 24, 2006. This transcript has not been reviewed for accuracy and has not been approved by the CDHS HSCR Advisory Committee.

STATE OF CA-HEALTH SERVICES

Moderator: Shabbir Ahmad
February 24, 2006
1:00 pm PST

Coordinator: The recordings have begun.

John Simpson: We're hearing nothing. I don't know if there's - something is going on…

Coordinator: Unfortunately, his line just disconnected. We'll have to wait till he dials back. And I do apologize.

John Simpson: Okay.

Coordinator: Please stand by for the conference to begin. Thank you.

John Simpson: Thank you.

Woman: May I ask you a question?

Coordinator: Yes, ma'am. Go ahead.

Woman: Is there a way to mute the line?

Coordinator: Yes. If you'd like to mute your lines today people, go ahead and push star-6 to mute, star-6 to unmute and toggle back and forth if needed to speak.

Woman: Thank you.

Coordinator: You're welcome.

John Simpson: This is John Simpson again. We're hearing nothing. Does that mean that the meeting place is disconnected?

Elizabeth Helen Blackburn: That's what it sounds like because we were getting some intermittent sounds earlier on that sounded as though we were being connected to a large room.

Shabbir Ahmad: …Department Health Office…

Coordinator: Sir, the conference recordings have begun.

Shabbir Ahmad: …California Department of Health Services (unintelligible)…

Coordinator: Excuse me sir, this is the coordinator. Everyone online is unable to hear you. You're coming in very muffle.

Shabbir Ahmad: Hello? Can you hear?

Coordinator: It sounds very, very far away.

Man: And very intermittent.

Shabbir Ahmad: I will speak a little louder.

The Human Stem Cell Research Advisory Committee was appointed by the Director to implement the statutes of Senate Bill 322 by Senator Ortiz.

I also want to extend my thanks to Advisory Committee members for their willingness to serve on the Human Stem Cell Research Advisory Committee. I would like to thank Professor Alta Charo for bringing the wealth of knowledge and experience from both National Academy of Scientists and California Institute of Regenerative Medicine, and many of those committees to this committee.

I also would like to thank our guest who would join us today either in person or via conference call.

For those who are on the conference call, there is a star-6 option if you want to mute and unmute your phone. I just prefer those who are on the conference call if they can hit their phone mute by pressing the star-6 to avoid any disturbance.

The meeting is divided into two parts. As you see from the introduction, the first part is the introduction, the charge of the committee, then few business highlights on the topic (interest forms), policies and disclosures. Then, we will be discussing the - and working on committee bylaws. And all of these documents are in your folder. And then we will elect the Chair and the Vice Chair of the Committee.

After Chair and Vice Chair have their speech, I will (handle) the committee proceedings through the Chair and Vice Chair and I would just become the facilitator of the meeting at that time.

The second part of the meeting is there will discussion on National Academy of Science guidelines and recently told CIRM regulation. There would be a committee discussion on those. Then at the discussion of the Chair and Vice Chair, there will be a break for 5 to 10 minutes, and then committee discussion of internal adoption of National Academy of Science and (CIRM centers), and then Dr. Magnus will provide us input on some of the areas which needs proper attention and discussion.

And there will be a time for public comments and then we will discuss when we will have the next meeting.

I will start with a short presentation. First, I will be (showing a) few slides and then followed by (Cindy) giving the process of the committee which is mostly part of the bylaws.

John Simpson: We seem to have lost everything again.

Shabbir Ahmad: …So the legislative history on California Stem Cell Research started (unintelligible) some of the bills and resolutions which I've mentioned over here, not all of them but the experience on (CIRM) has been 253 Ortiz is the message that state policy that both permitted stem cell research and prohibited the sale of embryonic or fetal tissue.

And then followed by Proposition 71, established (unintelligible) and required advanced directors for (unintelligible) during the facility treatment.

And then the Senate Bill 322 by virtue of this committee was appointed by the (Center) of the California Department of Health Services to develop centers for human embryonic stem cell research in the States.

In addition to developing the centers, the charge of the Department of Health Services under this bill is (unintelligible) stem cell research in California, review (unintelligible) and report annually to the legislature.

Then after this bill, it was 2004, Proposition 71 that authorize (unintelligible) internal obligation was to provide the funding for stem cell research and research facilities in California, establish the California Institute of Regenerative Medicine.

Very recently, there was a draft resolution by Senator Ortiz that - that was in September of last year that memorialize progress and (unintelligible) US to, number one, lift restrictions on federal funding of stem cell research; number two, not (interfere) the ability of researchers to conduct stem cell research applications that hold promise for developing (the copy) for treating and (doing) chronic diseases; and the third, develop ethical guidelines for currently funded stem cell research and for prohibit human cloning.

This (Act 1260), the last bill, this is just introduced on May 9. And if some of you can recall SB 18 where there were an informed consent from the egg donor, as well as audit of CIRM. That bill was vetoed by (the Governor) last year.

Senator Ortiz and (Governor), they introduce this bill on February 9. And that would require physicians to obtain written consent, as well as provide a standardized written summary of health and some human issues to patients undergoing assisted oocyte production for the purpose of donating eggs for medical research or developing medical (parties).

This bill might add additional duty if it passes through the assembly Senate and Governor Office. There would be some guidelines that need to develop around the cell or oocyte donation.

I already talked to Professor Greeley and he will update basically on that.

(Unintelligible) the task under the Senate Bill 322 by Senator Ortiz, there's a discussion for 125118 to 125119.5 to get a California Health and Safety Code Chapter 506 (unintelligible) the Department of Health Services. And there are five tasks -- established a Human Stem Cell Research Advisory Committee consisting of 13 members representing the professional (specialties) as specified in the statute.

Second task, develop statewide centers for human embryonic stem cell research which is the main task of this committee.

And the third, Department of Health Services would be collecting the mandated policy (forms) from all institutional review boards in California regarding the status of approved projects and proposals involving the stem cell research.

And I will mention that Prop. 71-funded a research would not come under the SB 322.

Review all IRB reports and revise guidelines as (set forth).

Number five task is to report annually to the legislature on human embryonic stem cell research activities in California.

The intent of (SB 322) was to provide uniform - I underline - underscore uniform statewide guidelines and centers at the labs to ensure comprehensive monitoring and recording of all human embryonic stem cell research in California.

So, after (SB 322) Proposition 71, some of material features of that initiative which was approved in 2004 (ballot) created constitutional (wide) to conduct stem cell research in California, authorize the sale of $3 billion in state (unintelligible) over ten years to fund stem cell research and research facilities in California, establish the California Institute of Regenerative Medicine and a 49-member Independent citizens Oversight Committee -- I talked to (unintelligible), prohibited CIRM funding for human reproductive cloning research.

Prop. 71 also included the language that practically accepted to serve (unintelligible) from the provision of Senate Bill 322, as well as any other current or future state laws or regulations (unintelligible). Also, certified that CIRM will develop its own scientific and medical standards.

(So) SB 322 today, while funding and other issues have (unintelligible) to implement the statute of Senate Bill 322. After the Prop. 71, the statute of 322 currently applies to all non-CIRM-funded research in California including DHS treatment, as well as stem cell research guidelines. We've mandated (unintelligible) advisory report in California and the annual report to the legislature.

Under SB 322, as implied by the statute, this Committee - an Advisory Committee was appointed by the California Department of Health Services Director. And according to the statute, this would be (unintelligible) with experience in environmental research in the field of cell transfusion, nuclear

reprogramming, tissue formation, (biology formation), stem cell biology, development biology, regenerative medicine (unintelligible).

And two seats will be occupied two medical officers. In addition to those (nine), two (unintelligible) background in legal issues related to human embryonic stem cell research in tissue fertilization or (certainly) law as it applies to donation of embryos.

And those 13 members, (our two questions) were the members of - leaders of religious organizations.

And this is the committee. I will - for the sake of record, I will speak their names.

Dr. Elizabeth Helen Blackburn representing (unintelligible)…

Elizabeth Helen Blackburn: And here on the conference call.

Shabbir Ahmad: Second, Dr. (Kevin Casher), Dr. Gregory Stock, Dr. Irving Weissman. Dr. Otoniel Martinez Maza, Dr. Fred Gage, and Dr. Bertram H. Lubin, all representing the field of Science Committee.

Dr. Hank Greeley - Professor Hank Greeley and Professor (Gogh) - (Danica Gogh) would be coming - bringing us the law background to the committee.

Dr. Bernard Lo and Dr. Magnus would be the (Access) Audit committee, and Dr. (Ernest Charles) and Dr. Margaret McLean, they would representing the (unintelligible) in addition to the committee.

I just want to mention over here that Dr. Blackburn, Dr. Gage and Dr. McLean, they would be driving us through the conference call today at different times according to their schedules.

Elizabeth Helen Blackburn: Yes, I'm here, Elizabeth Blackburn. I'm on the call.

Shabbir Ahmad: Okay, thank you.

What the charge of this committee? To recommend the Department of Health Services scientific medical tactical legal guidelines for research involving the (unintelligible) for use of human embryonic stem cells in California not withstanding the CIRM-funded project.

Just as a note, the committee providing the recommendations to the department final approval (unintelligible) guidelines adopted lies with the California Department of Health Services and the Health and Human Services Agency.

(Unintelligible) of this committee is the National Academy of Science guidelines that - those are released last year and then recently approved CIRM regulations by the ICOC on February 10, and then Advisory Committee recommendations.

And I think the goal of this committee is how all these guidelines (we have) compatible - they - we don’t want to have anything contradicting on each other and (unintelligible) the research of - in California.

From now on, (Cindy) is going to give a few slides information on the process which we will follow for the rest of the year for this committee and today.

And all of you know that this is a subset data on Senate Bill 322 which is January 1, 2007.

So (Cindy)?

(Cindy): Thank you.

First, (unintelligible) by the committee that this overseeing was developed based on our preliminary conversations with all of you (unintelligible) and that is (unintelligible) based on the committee (unintelligible).

That being said, the first meeting (unintelligible) policies brochure and both the committee bylaws, state nomination for Chair and Vice Chair and both the Chair and Vice Chair, (unintelligible) Chair and Vice Chair (unintelligible) the remainder of the meeting. And the goal of the remainder of the meeting will be to discuss (unintelligible).

(This) meeting, we expect to work from you to establish standards to develop the guidelines on these areas to (develop and) identify (unintelligible).

Again, this is a proposed timeline that (unintelligible) based on the committee meeting. So (we'll) anticipate at this point is that a draft guideline will be prepared by mid-August, followed by (unintelligible) public comment.

And the Department of Health Services will be (serving this) committee on all public (access) to the Department of Health Services Website and public (unintelligible).

And then having the final guidelines prepared by October 31 (unintelligible) approved the final guidelines before they are transmitted to the Department of Health Services (unintelligible) independent but supported by DHS.

So, the role of the Department of Health Services is to facilitate rather than to direct this work. So that means, with the approval of designated officers, the committee may set and modify some interim goals, agendas and assign people (unintelligible).

Likewise, we invite designated officers (unintelligible) executive coordinators (unintelligible).

(Unintelligible) Subcommittee present (specific debut). The (unintelligible) committee will be informal and chair the advisory to the full committee…

The work of the Chair and Vice Chair will be to coordinate the work of the Advisory Committee by leadership and (unintelligible) towards the committee to approve the recommendation to the Department.

So the work of the - coordinating work of the Advisory Committee entails calling (unintelligible), developing the agendas, (responsible for the) accuracy of minutes, (unintelligible) over the development of this committee (unintelligible) and final guidelines.

Chair and Vice Chair will provide (unintelligible) by providing a liaison (unintelligible) Advisory Committee and (unintelligible).

And finally, the Chair and Vice Chair will - as I mentioned, the role of DHS will be facilitate the (unintelligible) committee (unintelligible) the Vice Chair (unintelligible) development regarding public notice and also the committee

meetings and serving as liaison for the Advisory Committee and (unintelligible). (During the activity), the Advisory Committee (unintelligible).

We're also providing (unintelligible) set the final guidelines has been recommended and approved by the committee (unintelligible).

So that in a nutshell is the committee's charge and expectations of the committee. We are so excited that you're all here and really excited to work with you.

We would like to thank Dr. Lubin and Dr. (unintelligible) great job - contact information as well as the Website where (unintelligible).

Shabbir Ahmad: Well, I have given the charge the committee. And I think we can start with the introductions of the committee members here. And also for those who are planning (unintelligible).

So maybe, we can start from here?

Woman: (Unintelligible).

Shabbir Ahmad: I am Shabbir Ahmad. I am working with the California Department of Health Services. Currently, I am the Chief of Epi and Evaluation Section. And this is an additional task given to me last year to be the (Pro Tempore) Manager of the Stem Cell Research Unit. I will be working with you on this.

Before coming to California Department of Health Services, I work with (UT Davidson) for 15 years and worked on (unintelligible) molecular biology and

the disease around (unintelligible) work on AIDS vaccine development and (unintelligible) cytokine so - including the management (unintelligible).

So that's a little bit of my background…

Can you speak a little loud because I know that there are people on the phone as well.

Bert Lubin: Bert Lubin, I'm the President of Children's Hospital - university, high school…

John Simpson: We're having a great deal of difficulty hearing what's being said now.

Woman: Yes.

Bert Lubin: Well, we are doing the speaker.

Elizabeth Helen Blackburn: It's still breaking up.

Bert Lubin: So, I'll start again. I'm Bert Lubin. I'm the President of Children's Hospital Oakland Research Institute. And we're sitting in a building a 100,000 square feet of laboratory space. It was a high school built in 1917 and is completely occupied. Now, the rest of the campus outside is run by the Children's Hospital. And the building that you walk by the gym, it says, "Boys and Girls," was the gym and the school was built in 1917.

And we're very happy to have all of you here and host this first meeting.

I'm a pediatric hematologist and my research interest currently relates to stem cells and cord blood banking of course by use of cord blood for transplantation.

Irving Weissman: I'm Irv Weissman from Stanford University. I'm Director of the Institute for Stem Cell Biology and Regenerative Medicine.

My own research is on adult or tissue-specific stem cells. I am also a Director and Founder of two companies in the stem cell arena, both adult or tissue-specific stem cells -- one called (Celerant) for blood-forming stem cells, another called StemCells, Inc. for human brain stem cells and human liver stem cells.

So, obviously, during the discussions, I'll have to let you know where I think the conflicts might arise.

(Sam Leticia): I'm (Sam Leticia). I am from Stanford University (unintelligible) Neurological Surgery. My past research included learning about the cell psychokinetics of (unintelligible) stem cells. I actually got my PhD in Dr. Weissman's laboratory.

And my current research includes isolating the cancer stem cells which are responsible for human brain tumors.

(Wanda Carell): I'm Professor (Wanda Carell) and I teach at the University of California teaching College of Law in San Francisco. My areas are Property, Constitutional Law and Law and Medicine. I've been doing research in issues such as cloning, stem cell and genetics.

Elliot Dorf: I'm Elliot Dorf. I think I'm here because I'm a Rabbi and I do a lot of Jewish bioethics. But I also have a Doctorate in Moral Theory from Columbia - Doctorate in Philosophy from Columbia with a dissertation on Moral Theory. And I've done a lot of work in the ethics and bioethics. I've been in several government commissions (sort of federal) government, and I could be on this one.

Otoniel Martinez Maza: I am Oto Martinez Maza. I'm an immunologist at UCLA. My research interest is pathogenesis of AIDS-associated cancers. And I'm a member of both our Cancer Center, as well as our AIDS Institute.

Gregory Stock: I'm Gregory Stock. I direct the Program on Medicine, Technology, and Society at the UCLA's School of Medicine. I'm presently in the Department of Pediatrics there.

I also am the Founder of a biotech company called Signum Biosciences which is developing pharmaceuticals for Alzheimer's and a new class of anti-inflammatory drugs. And I have written fairly extensively about the implications of new technology of sort of the breakthroughs that are occurring in the life sciences and what the implications are for medicine and for society as a whole.

And so I've been participant in the debate about stem cells and cloning for some time.

David Magnus: My name is David Magnus. I'm Director of Stanford University's Center for Biomedical Ethics. I'm a faculty member of the Department of Pediatrics. I Chair the Ethics Committee for the Stanford Hospitals and Clinics. I've written about a range of issues especially concerning genetics and stem cell

research. And I'm also one of the editors of the American Journal of Bioethics.

Hank Greeley: My name is Hank Greeley. I'm a Law Professor at Stanford where I'm also Director of the Stanford Center for Law and the Biosciences and Director of the Stanford Program on Stem Cells and Society. My research over the last decade or so has focused on ethical, legal and social implications of advances in human genetics and neuroscience, to some extent in (essence of) reproduction.

I've had the pleasure of serving with some of the other committee members on the California Advisory Committee on Human Cloning which issued its report on January 2002.

Shabbir Ahmad: (Unintelligible) on the phone, please introduce yourself.

Elizabeth Helen Blackburn: Shall I start?

Hello? Can you hear me?

Shabbir Ahmad: Yes, go ahead.

Elizabeth Helen Blackburn: I'm Elizabeth Blackburn. I'm at the University of California, San Francisco where I am a Professor in the Department of Biochemistry and Biophysics. And I also serve on UCSF Gamete, Embryo and Stem Cell Research Oversight Committee that's chaired by (Bernie Lowe).

And my own research is on the cell biology and molecular biology aspects of cells including aspects that are relevant to stem cell biology. I am also a member of the UCSF Cancer Center. I've served on a Federal Advisory

Commission that was the President's Council on Bioethics in 2002 to 2004. And so stem cell issues were discussed at the Council.

Yes, that's it.

Woman: Would you like to introduce yourselves - other participants on the call?

Shabbir Ahmad: Others from the phone who want to introduce?

Nicole Vasquez: Sure. This is Nicole Vasquez. I'm with Senator Ortiz's office, Senate Health Committee.

Thank you for having me.

Shabbir Ahmad: Thank you.

Anyone else on the phone?

John Simpson: Yes. This is John Simpson. I'm with the Foundation for Taxpayer and Consumer Rights. I'm the Stem Cell Project Director there.

Shabbir Ahmad: Thank you.

Anyone else on the phone?

Susan Fogel: Yeah. This is Susan Fogel. I'm the Coordinator of the Pro-Choice Alliance for Responsible Research.

Shabbir Ahmad: Thank you.

Anyone else on the phone?

Shannon Smith-Crowley: I'm Shannon Smith-Crowley. I'm lobbyist for the American Society Group (unintelligible) Medicine (unintelligible) OB/GYN.

Shabbir Ahmad: Thank you.

Next on the phone?

Thank you.

And I'm also ask Dr. (Charles) to introduce…

R. Alta Charo: I'm Alta Charo. I'm a Professor on the (Cohesive) Law and Medicine at the University of Wisconsin. I'm visiting at the University of California Berkeley Boalt School of Law this year.

My scholarship has focused for years on reproductive technologies law and on science policy and the politics of bioethics. In the areas on where research and stem cell research I've served on the NIH Human Embryo Research Panel in 1993, on President Clinton National Bioethics Advisory Commission from '96 to 2001 which wrote on cloning and stem cell policy.

And I serve as the liaison from the Board on Life Sciences to the NIH Committee on the development of guidelines for human embryonic stem cell research, currently serving on the Standard Working Group for the California Institute for Regenerative Medicine.

And also, just by way of revelation for conflicts purposes, I also on the Bioethics Advisory Board for the Juvenile Diabetes Research Foundation

which does fund in the area of embryonic stem cell research and the Bioethics Advisory Board for the International Society for Stem Research which is in the process of trying to develop transnational guidelines for recognition of one another's ethical standards for stem cell research.

((Crosstalk))

Man: It's not a bad thing…

Irving Weissman: I was - this is Irv Weissman. I was also Chair of the National Academy panelists on the scientific aspects of human reproductive cloning and its relationship in stem cell (unintelligible).

Shabbir Ahmad: Any (other) just to want to introduce themselves?

Robert Price: This is Vice Chancellor Robert Price. I'm the Associate Vice Chancellor for Research at UC, Berkeley.

Geoffrey Lomax: Geoff Lomax, I'm the Senior Officer from the California Institute of Regenerative Medicine. I'm in charge with facilitating the working group…

Jesse Reynolds: Excuse me. I'm Jesse Reynolds with the Center for Genetics and Society.

Man: Hi, Jess.

Man: Hi, Jesse.

(Kurt Franken): My name is (Kurt Franken) with the California Institute for…

(Peter Sherman): My name is (Peter Sherman). I'm the Director in (Industry Alliance's) Office.

Man: (Unintelligible).

Shabbir Ahmad: Hello?

Fred Gage: Hello?

Shabbir Ahmad: Hello?

Fred Gage: Yeah. This is Fred Gage.

Shabbir Ahmad: Thank you very much. Welcome. Yeah. We are introducing ourselves at this moment.

Can you go ahead and…

Fred Gage: Yeah. I was - yeah. This is Fred Gage from the Salk Institute. I'm in the Laboratory of Genetics and Director of the Salk Institute Stem Cell Facility. I am also declaring that I have affiliation with two biotech companies that are involved with stem cells in one or another -- one is called StemCells, Inc. in the Bay Area, actually in Palo Alto; and another one is called (PCI), which is involve in adult neural stem cell here in San Diego.

My own research deals with adult neural stem cells but also, I work with human embryonic stem cells and fetal stem cells. Our goal is to understand the mechanisms by which an undifferentiated becomes a functioning neuron.

Shabbir Ahmad: Thank you.

We are going to go to next agenda item which are the proposed conflict of interest policy and the disclosure form, and also proposed committee bylaws.

We - those who are like they approve those - that policy and the form, they can sign it today or they - if it is not approved today then we can have some discussion on it today and have approval and signatures on the form (unintelligible).

So it's open for discussion at this moment, especially the conflict of interest policy and form.

Just to let you know that we took basically National Academy of Science and CIRM as a model for developing this policy and the disclosure form.

Man: I just wanted to say that I think the disclosure form and the policy in the disclosure form was fine to me. I hope we all recognize that many of us will have things that are conflicts one way or the other which is not necessarily disqualifying some membership but may affect our ability to bode on any of the individual matter.

And I would suggest and encourage people to take a broad view of what…

For example, it asked about our employer's interest, my employers at Stanford University. It has potentially financial interest in human embryonic stem cell research, so we'll note that as a potential conflict even though out of the $2.6 billion annual budget of Stanford, it's hard to imagine that this is significant and as I said you remember law of faculty, it's hard to imagine that the medical school could have any influence over my decision-making.

But I think it's still better to look at these things broadly and encourage everyone to do that.

Shabbir Ahmad: Thank you for the comment.

Any other comments on conflict of interest form, employer's policy?

I think there's no…

Woman: Could you please identify yourself when you speak?

Shabbir Ahmad: Okay.

Woman: Thank you.

Shabbir Ahmad: Thank you.

Shabbir Ahmad. It seems like that we have the policy and the form approved by the committee at this moment.

Man: I move that we approve the policy and form of conflict of interest and disclosure.

Man: I second.

((Crosstalk))

Shabbir Ahmad: Okay. So - and those who are in favor?

Man: Aye.

Woman: Aye.

((Crosstalk))

Shabbir Ahmad: Yeah, those people who oppose say nay?

So it's approved unanimously. Thank you very much.

And then also the committee bylaws, the - those bylaws - this is Shabbir again. Committee bylaws, they are modeled on the National Academy of Science and also CIRM. So if there is any discussion on those, please - pardon?

Man: I move we accept (those).

Shabbir Ahmad: Okay. There is move (unintelligible).

Any second?

Those in favor say…

Man: Well now there's time for discussion for the motion if anyone has any discussion about this motion to accept the bylaws?

Shabbir Ahmad: (What's supposed) the discussion? So motion for accepting those bylaws?

Man: We'll go through (unintelligible).

Shabbir Ahmad: Okay.

All those in favor?

Man: Aye.

Man: Aye.

Man: Aye.

Woman: Aye.

Shabbir Ahmad: Those in - those who oppose say nay?

So these policies and bylaws are approved unanimously.

Now, we are going to have nomination for the chair of this committee.

Man: I nominate Hank Greeley.

Shabbir Ahmad: Any second?

Woman: I second.

Shabbir Ahmad: So, any other nomination?

So...

We can do separate, yeah. Okay.

So the motion is that Professor Greeley is the Chair of California Department of Health Services, Human Stem Cell Research Advisory Committee.

Any - I mean therefore yes?

((Crosstalk))

Man: Aye.

Man: Yes.

Man: I vote yes

Shabbir Ahmad: Okay.

And those who oppose?

Hank Greeley: Nay. It's Hank Greeley voting no.

Shabbir Ahmad: So with the one nay, we have Professor Greeley as the Chair of Committee.

Man: I will move the discussion to move that if in fact Professor Greeley doesn't want to be the chair, then I think…

Hank Greeley: I'm willing to accept as long as I can vote against myself.

Man: Thank you.

Shabbir Ahmad: I need now the nomination for the vice chair.

Woman: I nominate Bertram Lubin.

Shabbir Ahmad: The motion is that Dr. Lubin would be the Vice Chair of the California Department, Health Services Human Stem Cell Research Advisory Committee.

Those who are in favor say yay?

Man: Yeah.

Man: Aye.

Woman: Yay.

((Crosstalk))

Shabbir Ahmad: And then those who oppose say nay?

Okay, so we have unanimously approved Dr. Lubin as Vice Chair of the Advisory Committee.

And I hand over the - now the committee proceedings to Professor Greeley.

Hank Greeley: Thank you, Dr. Ahmad.

I sort of want to thank those of you who voted in favor of me being chair. I fully realized the motives involved in anyone not being (wanting) to be chair themselves, and appreciate the intelligence of those motives.

What we've got on schedule for the rest of the meeting as the discussion of the CIRM guidelines and the NAS guidelines presented by Doctor - Professor Charles who's been instrumental on the creation of both, and then a discussion for Dr. David Magnus of some presumed or apparent possible gaps in those.

I guess I'd like to say that I don't know that we'll need to go to 5 o'clock with this meeting. And if we don't go to 5 o'clock, I won't count it as a failure or loss.

I also suspect that we may not have to have very many meetings of this committee. We have an important role, but I think it's a relatively limited role, SB 322 deals only with human embryonic stem cell research in California. It does govern research that is not covered by the CIRM and Prop 71 because it is not funded by CIRM. It also covers research that is not necessarily covered by the common rule, if it's done without federal funding o at an institution that doesn't - hasn't given the federal government an assurance of compliance with the common rule.

It's certainly going to be important for us to be at least consistent with the CIRM regulations, interim regulations. Nobody wants to put researchers in a position of having to do two completely mutually inconsistent things.

There may be some - there may or may not be some ways in which we want to go beyond what the CIRM has done. I think that's part of what we need to discuss today.

So, unless there are other general comments from the group, and I see one hand, Dr. Dorf.

Elliot Dorf: (unintelligible), so I'm going to have to be back on Los Angeles by sunset today. So that means I'm going to have to leave in 20 minutes, so - with your permission. But if we could set the next meeting now that would be good.

And I have some comments on these guidelines. If you'd like me to state them before I leave, I'd happy to do that, otherwise I could just email it to you if you like.

Man: (unintelligible) your comment?

Elliot Dorf: There are four of them basically.

Man: Why don't you put it on the table now (unintelligible) if you need to leave before - leave in order to arrive home before (sun down).

Elliot Dorf: Okay. One issue is just simply how realistic it is to expect women to donate their eggs free of charge. That the UCLA Bruins -- I can't say the law school at UCLA -- every single time, there are ads for women to donate their eggs for purposes of fertilizing other couples. And while the standard used to be $5,000 plus expenses, I've seen ads as high as $80,000 for a particular kind of egg.

And so one issue that - I mean I understand why the guidelines don't want to have any exchange over this, but if the case, I'm sort of wondering whether is it at all realistic.

(unintelligible) we might ultimately be having guidelines for the null set in which is I think problematic.

The second thing was on Page 6 for women providing oocyte. It's - what is this? A hundred thousand eggs of B2 - B1 for women providing oocytes for research and clinical and fertility treatment, either for herself or other women, research shall not compromise the optimal reproductive success of the woman in fertility treatment.

My question is how is that supposed to be demonstrated? The fact of the matter is that you're introducing hormones to, in order for her to hyperovulate, and that inevitably is going to have some effect on her and perhaps on her ability to reproduce.

And so if, you know, how is that - what are the standards for demonstrating that it's not going to have that effect?

Third thing on Page 8, it's 4D. Whether that the woman is supposed to be told whether stem cell line will be derived from their oocytes through fertilization SCNT pathogenesis or some of other method. I'm not complete sure why she needs to know that. I doubt first of all that somebody who's not used to these terms or to (unintelligible) all together would understand them. But aside from that, what relevance does that have to her donation?

I mean I think other things are relevant to her donation in terms of how it's going to be used. But this specific methodology by which her oocytes are going to be handled, it seems to me it's just not up to something that she needs to know.

I don't think it harms her to know it, but I don't know that she's going to gain very much from knowing it.

And then finally, my last comment is that there are two things in the guidelines for human embryonic stem cell research that we got from the National Research Council and Institute of Medicine that are not in these guidelines that I think probably should be.

On Page 91 of those guidelines, their (number K) there I think is important -- A statement that neither consenting nor refusing to donate embryos for research will affect the quality of any future care provided to potential donors. I think that's critical and it ought to be in these guidelines.

It's again the Recommendation 19 at the bottom of the page.

And then the next page, the other thing that I think would be good is clinical personnel who have a conscientious objection to human embryonic stem cell research should not be required to participate in providing donor information.

There's nothing as far as I could tell in the current guidelines having to do with the clinical personnel involved. And that I think - you know, you might say, well they shouldn't take the job if they want to do this, and there's something to that frankly. But I think it seems to me that if they're going to be involved in any way (they) perform, there has to be at least some provision for being able to simply opt out of certain pieces of it.

Those are my comments.

Man: Just for purpose of this clarity, I think you were commenting with respect to the interim CIRM guidelines.

Elliot Dorf: Right. Yes.

Woman: Yeah.

Man: So in a way that makes it my segue because I Dr. Charles is going to talk about CIRM guidelines and NAS guidelines. And also if we could impose upon you to reflect upon Dr. Dorf's concern in your presentation…

R. Alta Charo: Sure.

Man: …I think that would work out well in terms of timing.

It may mean that you're not going to be able to hear the full discussion of that today.

R. Alta Charo: …that are currently subject to public comment.

Two of your concerns have already been addressed, specifically the kind of conscientious refusal is included, and the promise to couple that refusing or consenting to donate has no effect on care also specifically included. So at least those two elements have been addressed, the others, no.

Elliot Dorf: Here's a question of what is regulated by the guidelines. And what about research which is both funded by embryonic stem cell money that's been allotted by the state and that is required - is funded with some measure of other…indirect funding or, I think would be most money that would be missed. Then that case it seems to me that there will be a question as to whether this would apply.

Man: Without wanting to give a formal legal opinion, I'm happy to say that I think that's a really interesting and complicated question. The CIRM Prop 71 says that research with CIRM funding will not be subject to this. If the research

has two streams of funding, is this all - whether that applies fully I think would be an interesting question.

Elliot Dorf: My point being that…

Man: I hope that we won't actually come to that. The two sets of regulations are mutually consistent and reinforcing it shouldn't matter.

Elliot Dorf: My point being that the scope of regulation - the scope of what this applied to could be larger than you would initially imagine.

Man: Yeah, that's certainly…

I guess I would also note here that there is another Californian statute, one that was definitely in the introduction. SB 253, which I believe is also Senate Ortiz Bill of 2002, which applies beyond embryonic stem cells to a fetal stem cells, umbilical cord stem cells, and adult stem cells and requires IRB approval for any research. That is not however part of SB 322 and not part of the guidelines we're supposed to come up with.

So, there are some state regulation going beyond embryonic stem cells, and the of course the CIRM guidelines will also apply to the extent they fund research beyond embryonic stem cells into other stem cells.

But as I read SB 322, our mission is limited solely to human embryonic stem cell derivation and use.

Gregory Stock: One further point before Dr. Charles begins her presentation is I also share the concern of Rabbi Dorf about the prohibition of remuneration for the donation

of embryo which you pointed an obvious reason that that is problematic and that there is a market for the services at a higher value.

The other is that if you have any experience with what is required in donation, not like (unintelligible) donation where there's not a - there's significant reasons why one would not do it casually. And so I'm wondering whether the identification of that as an issue that needs to be seriously discussed if we shouldn't have that discussion while Rabbi Dorf is here as opposed to at a later point when we were going to identify areas that needed further discussion.

Woman: Could you please identify yourself when you speak for us on the telephone. Thank you.

Man: (unintelligible).

Man: I guess I think that given the very short period of time before Rabbi Dorf has to leave that I understand and I appreciate what's driving your question, Greg, but I think we'd be better of going directly (unintelligible) presentation.

I suspect we will return to this issue at a subsequent meeting. I don't anticipate that we'll have very many subsequent meetings, but we'll certainly have at least one and I'm guessing maybe two, possibly as many as three.

This strikes me as an issue that would be good for us to discuss after we've heard a little bit more about the current guidelines and perhaps after a working group or sub-committee of this group has given some more thoughts to what might appropriately be done by this committee on this issue.

Man: Are there any other questions or comments from committee members before we turn to Professor Charles?

Man: (Eventually) in the next meeting.

Man: Can we realistically do ahead of meeting? My experience has been that scheduling meetings is so horrifically difficult these days that it takes extensive rounds of email discussion. I'm not sure we can actually realistically do this. Professor Weissman?

Irving Weissman: No, I just wondered if…

Man: I think…

Irving Weissman: That's (unintelligible), right?

Man: Probably one would be okay, but…

Man: Yeah.

Irving Weissman: I think we should be talking.

Man: I think we should make every effort to schedule the next meeting in a way that does not conflict with anybody's religious obligation. And I thank you very much for being willing to come up for such a short stay.

Other comments before we move on?

Dr. Lubin?

Bertram Lubin: This is sort of in building - my cell phone is not working through. We have to go outside. If your phone rings, (unintelligible) answer the call in a restroom or right outside the hallway there to right.

Man: While we shouldn't think that they - I don't believe there might be - this might be a good forum to get a sense of where the meeting might take place because there probably easy way to decide where it might occur if you think that is an appropriate topic for discussion.

Man: I guess I don't have any strong view about that. We probably have to choices -- Northern California and Southern California with apologies to my fellow citizen Modoc County and Yuma -- I guess Yuma is in Arizona -- whatever the California town is close to Yuma.

I think it probably all other things being equal would be nice to have the next meeting in Southern California. I do think we have disproportionate number of Bay area citizens here, Bay area residents on the committee.

Greg, I think this is something that probably makes sense to try to work out as we go through emails and so on. And also, some people would be able to make meetings on day in one location but not necessarily the others.

But just as - I think we should be considerate of religious and other time constraints on members, it would be nice, all other things to be close to equal (unintelligible) the meeting in Southern California, all other things...

Man: Oakland is fine. Sacramento would be a little bit (unintelligible).

Man: No comment.

Gregory Stock: Other questions or comments before we move to Professor Charles?

No? Well in that case, I'm very grateful that Alta was willing to make this presentation. She's listed some of her many activities and accomplishments. But it's particularly noteworthy her significant involvement in both the National Academy Guidelines and as a member of the working group that set up the CIRM guidelines by giving her unparalleled expertise on the issues.

Dr. Charles? Professor Charles?

R. Alta Charo: Thanks, Greg.

My understanding is that the levels of familiarity with the details of the laws and regulations here vary a bit, but clearly nobody hears it and complete naïve.

And so what I'd like to propose to do is to walkthrough some of the origins of the legal questions, quickly review the highlights of the National Academy's report and the key attributes of the CIRM regulations that are about to go in to their public comments period, and then leave time for people to focus in on those things that are most - of most concern to this particular committee particularly in light of the stated goal of avoiding unnecessary conflicts among all these different forces of guidelines, unless the researches and the institutions we subject actually conflicting, not only redundant but conflicting procedural and substantive requirement.

So by way of background, it's worth noting that we are not without federal law on the subject of stem cell research generally and embryonic stem cell research in particular.

There are a number of federal laws not specifically aimed at this area of research but nonetheless do govern it in the various institutions where it's going on, regardless of whether it is funded by the NIH or by private source or by a state source such as a bond initiative like Prop 71.

For example, most although not all of the tissue donation that is involved in embryonic stem cell research and in adult stem cell research will necessarily involve what is now deemed to be a human subject of research. It's not the way human subjects commonly understood. These people are not (unintelligible) being studied but by virtue of the interaction with them, they're rendered in human subjects under federal definitions in most, although not all (representatives).

A key area where they are not rendered human subjects under current federal regulation is in fact one of the most typical circumstances which is the near donation of tissue where the tissue is (anonymized) so that subsequent work reveals nothing about the donors.

So for example a couple out in facility clinic that agrees to donate their embryos where those embryos are used to derive cell lines that are appropriately (anonymized), those donors are not going considered human subjects.

If however the cell lines retain key information about the donors and then link back to the actual identity of the donors in a way that makes their identity readily ascertainable, that then means that studying those subsequent lines by implication means studying the donors as well, and now you are govern by the federal regulation.

This is kind of complicated and somewhat anomalous area of federal human subjects protection law, and it's exactly why if we get into the National Academy and CIRM guidelines, we begin to see expansion of the general kind of human subject style oversight and protection of donors.

Similar issues arise when you begin to move into the donation of fetal tissue, cord blood and adult tissue as well.

Pertinent to that particular area of discussion as well or the intersections of the Food and Drug Administration regulations and the Federal Privacy Law, so called HIPAA, Health Insurance Portability and Accountability Act.

Food and Drug Administration regulates tissue transplantation. And so to the extent that stem cell research become a purely laboratory exercise, the FDA is really not involved. However, if stem cell lines are being used to develop transplantable tissue, then the FDA jurisdiction, because of its interest in the prevention of the spread of infectious disease goes through the very laboratory work and the storage condition, and even the donor's screening and identification and record-keeping of the original donation.

So in this fashion, although you may not know today that the work you're doing is going to be FDA regulated because you don't know today that the stem cell research you're doing is going to yield transplantable tissue three years from now from these cell lines, to some extent, you have to decide today whether when you're asking people for tissue or whether when you're (doing) tissue or when you're working with tissue in your laboratory, at every moment you have to ask, is there any possibility that the materials I'm working with will ultimately be used to develop transplantable tissue, because if they are, then I need to worry about the FDA's rule about donor screening for infectious disease, about record-keeping about donor identify so that you can

go back subsequently if you check on any further infections or genetic disorders that have been merged since the time of donation. You also have to worry about the FDA's rule good laboratory practice and good manufacturing practices, depending upon the particular end uses of your tissue

As a result, the FDA has - FDA's regulations have a very significant role to play in this area. And because of the intersection with donor - with donation and donor identify, it has a significant role to play also with triggering (some stem cell) human subject protection. Since the FDA wants information about the donors to be maintained so that they can track back from the cell lines with donor, they essentially undermine the possibilities of (respective anonymization) that would take those donors out of the human protection system.

So there is a bit of an inner plate here that has a bit of a circular quality.

Notice as well that as soon as you are retaining donor identity, you also need to worry about the privacy implication since the materials may give you probable list of information about the donor. And so therefore the HIPPA privacy law comes into play which has its own set of rather convulsant procedures by which people give authorization to have their medical records - medical information used and maintained - excuse me - or by which a separate so called privacy board can wave that requirement for certain kinds of research.

So, those institutions that are in the area usually have the general account comparing this (hereout) over making sure the HIPAA compliance is achieved.

In addition, for the purely laboratory research that goes on, there are federal rules that come into play with regard to specific kinds of experimentation that may go on.

For example, a great deal of the current stem cell research in United States involved some kind of genetic engineering of the stem cells, or it soon will require genetic engineering of the stem cells. And at that point, we have standing committees that look at all the experiments that involved genetic engineering. And these committees are organized locally through institution by a safety committee.

And at the national level, we have the NIH (recombinancy) in an Advisory Committee technically with jurisdiction only over NIH funded research practically exercising authority over pretty much all recombinant research in the United States.

Most of what is done in the stem cell field will be of the minimum risk with regard to the genetic engineering aspects, but nonetheless this is something keep track of.

Finally, much of the stem cell research that we're going to be seeing will necessarily involve some kind of combination of human and non-human tissue for example, by testing out how human tissue derived from stem cell - sorry - developed from stem cell will actually (graft) when place into a live animal at various developmental stages and in various organ system.

And in that case, we have standing federal rules that govern animal wellness. It doesn't cover every animal. There are specific animals that are on the list and others - other animals that are not. But many of the animals that might become of interest are in fact on the list. And so the transplant process and

the resulting combined tissue and its effects on animal since we experience it or even in some kind of theoretical mode that people worry about it, we've not seen yet, cognitive experiences would be inappropriate subject of discussion by the so called Institutional Animal Care and Use Committee, the IACUC.

Given that we had all of this regulation in place granted not specific to embryonic or adult stem cell research but nonetheless in place to the medical research generally, and given that we had human subject research rules that were largely going to be applicable either because the institutions have pledged to them for all even non-federally funded work or because the FDA donor screening rule has essentially triggered the applicability of human subject's rule, the question can reasonably ask, why do we need more?

And the answer in part lies entirely with the - in the world of public relations. This is an area of research that has engendered tremendous controversy, not only among people who fundamentally object to the destruction of human embryos, but also among people who simply worry about the way in which the science is progressing and the directions in which applications may take.

And so to that extent, it has some echo of the debate here in Northern California and elsewhere in the late 1970s over the origins of recombinancy in a research.

The only specific rules we have that really covered the issue of embryonic stem cell research in particular where regulations that were coming out of the National Institutes of Health. They focused on what the NIH would fund and what it would not fund. And here, it was very specifically and primarily at which lines it would fund. That is the crucial details about the line's origin.

This reflected then the President's policies do not fund research on lines created after August 9, 2001, and also very specifically said that the lines prior to 2001 that could be eligible for use in federally-funded research has to meet certain core ethical standards such as informed consent of the donor's non-payment for the lines and such.

That really gave very little guidance for what should be done with the newer lines that were being developed without NIH money.

It was against this backdrop. But the National Academy of Sciences created a committee following on its two committees, one of which slight mentioned earlier. Two committees that worked on the promise of stem cell research and another that worked issue surrounding reproductive cloning, which against the backdrop of the National Academy said that it was time to have a set of national guidelines as to how to conduct this research, guidelines that could be used by people all over the United States, and in this way attempt to sort of fill in the gap between the federal laws and regulations that existed on the general topics of FDA regulation, animal welfare, genetic engineering and such.

Second, increase public confidence in the management of this area of research.

And third, to facilitate collaboration among laboratories and across state lines and national lines by harmonizing the core ethical standards, something which was important for facilitating research because each institution and each state was beginning to develop its own sets of standards and its set of procedures, putting institutions at risk of being unable to efficiently comply with all the different rules, and thus preventing people from sharing lines collaborating on experiment.

In order to then meet these goals, fulfilling the gaps, increasing public confidence and facilitating collaboration through harmonization of standards, the National Academy report, which I think you've all received, came to the following kind of core sets of recommendation.

First, that there ought to be added a new distinct level of oversights through something that it called the Embryonic Stem Cell Research Oversight Committee, the ESCRO.

This was one of the most important and most controversial recommendations. The creation of yet another bureaucracy was not necessarily welcome by the scientific community, and yet it was a recommendation that was (arrived at) in large part because no existing entity appeared to have either the expertise or the time and resources, or the overall jurisdiction to essentially gather within it in one place a comprehensive review of the research that would allow for a single process, for oversight and record-keeping of single process, for advising on particularly difficult and ticklish question, and a single place where public input could be focused.

And I'm going to come back to this because this ESCRO requirement which is reflected again in the CIRM regulation hovered the challenge for this committee because of the state law that it is working under that - it appears, what I'm going to defer to Professor (unintelligible) and Greeley on on this - appears to require specifically IRB review of all stem cell research, even apparent with stem cell research not involving human subject, whereas the NAS report would reserve the non-human subject aspects of this research to this separate specialized focus committee called the ESCRO. So this already is one area in which there is something to be not managed.

Second, the National Academy report recommended expanding the IRB's jurisdiction with regard to human subjects research to very clearly include oversight of the donation of tissue. Now remember, the NAS reports on human embryo on a stem cell research only, so it's not talking about donation of fetal tissue, not talking about donation of cord blood, and not talking about donation of somatic cells or bone marrow for adult stem cell research.

And the area of embryonic stem cell research, however, recognizing that there would be circumstances in which the donors of surplus embryos would not be considered human subjects and where the donation process therefore would not necessarily be given overseen by an IRB, the NAS recommended that IRB nonetheless take on this path and that institutions allow them to do so.

Institutions aren't required to under federal law, but they are permitted to expand the jurisdiction of their IRB on their own initiative.

Third key area of the NAS recommendations was the proposal that there'd be substantive limits on some forms of laboratory research and not substantive for provisions but forth conversations prior to commencing other areas of research.

And I'm going to - I'm going to circle back to that again with the CIRM guidelines because they are reflected there as well.

Finally, and this kicks up on Rabbi Dorf and Dr. (Sacks) comments about payment to egg donors. There is a recommendation of the National Academy's report that the donors of (gammi) -- that would include sperm as well as egg -- not be paid for the donation if it's being made for the purpose of developing a new entity from which stem cells are going to be derived. For

example, if you're using them, egg for SCNT work or sperm and egg to use IBS to create an embryo from which you were going to derive new line.

These two was the focus of tremendous controversy and great deal of comments during the review period for the National Academy's report. If you read the report, you'll see arguments laid out for and against (unintelligible) payment. And you will also see the conclusion. And this is important too because it's a recent event in the United Kingdom.

You will also see the conclusion that if you keep in mind the goals of the National Academy's effort which was to fill the gaps and the regulation, increase public confidence and to facilitate collaborations and harmonization, that the second two goals were furthered by prohibiting payments.

The reason being, first, there was a portion of the public opposition to some stem cell research, particularly cloning research that was coming from people who's claim had been that they're primary concern had been that women would be unduly enticed to donate eggs and that this was a risk that was not worth taking for money.

Whether you would agree or not, it was a source of (persistent) criticism and one issue with public confidence is in reassuring people that their concerns are being addressed.

The second was the facilitation of collaboration. The time the National Academy's report is being written, the United Kingdom had a practice of not paying for the donation of any egg or sperm or embryos obviously, and the same limitation was present in all the other major centers of embryonic stem cell research, and Prop 71 (unintelligible) with a specific prohibition within Prop 71 on the payment to egg donors.

Now if we have a situation in which across the country and across the globe we have some stem cell lines that were developed with materials that were purchased and other stem cell lines that are developed with materials that were not, we run into them the question of whether or not any one institutional state or country is going to forbid their researchers from importing and using or even collaborating with somebody who uses the line but fails to meet their standard. That is imaging the question of whether or not a California researcher could possibly be forbidden to collaborate with somebody, let's say, from Massachusetts because the Massachusetts researcher is working with the line that came originally from paid egg whereas the California researcher was not.

This issue is kind of common plates for lawyers who have whole courses about the problem of the conflict of laws and when you recognize and accept that in people's laws and when you simply put this down and say it's my way or no way.

But in the scientific community, I think this problem was a little more novel, and I don't think its implications and clarifications were fully appreciated by everybody as they debated the issue with egg donation.

So I'd only emphasize to you that as we continue the discussions because it's a very worthy discussion with reasonable people in all sides of the subtenant question of paying for materials that you also keep in mind the other goals of the system besides a kind of principled approach to each individual issues such as payment, and also keep in mind the goal of making sure that the research goes forward as efficiently as possible so that we actually achieve some therapeutic breakthrough for the patient population. Now once the National Academy document with issue, it became a subject of a great of

discussion. And in California, with the California Institute for Regenerative Medicine or CIRM was working towards writing regulations for its own funded researchers, it became to many people a jumping off point for discussion.

I'd like to now take some time to just briefly walk you through the highlights of the CIRM regulations that are available for public comment and then allow you all to guide the discussion wherever you think it needs to go. And so for this, there's a handout which is a printout of those CIRM recommendations.

First and very importantly I want to note the following. The CIRM regulations are not regulations that say this is how stem cell research should be done. They are regulations that say this is what we will fund and this is what we will not fund.

State law is perfectly free to be more liberal on any number of things about what people can do. CIRM simply will choose not to fund some of those activities. So in some ways liberalizing the (unintelligible) of standards is unproblematic. It's the procedure in many cases that must be harmonized in order to make sure that the institutions don't have an impossible or inefficient bureaucratic task.

In other cases you do want the (unintelligible) standards also to be the same if you're aiming for efficiency. But I did want to emphasize that the CIRM standards, unlike the National Academy's which would (unintelligible) to tell people how they ought to behave. Wherever you are, wherever you do, do it our way. That was the National Academy.

CIRM's goals was - were modest and that was if you're going to use my money, you're going to do it my way. And in that sense, it was an echo of the

federal government's decision to fund only some forms of research and not others.

Next I want to highlight for you that unlike the National Academy's report the CIRM regulations specifically address all forms of stem cell research and not merely embryonic stem cell research.

This is crucial because not only is CIRM planning to fund in all those areas but it also I think helps to add an important concept and that is that stem cells are important because of their plasticity. It's the plasticity that creates some of the interesting dilemmas when we get to laboratory research, the creation of chimeras or ultimately down the line of therapeutic interventions involving transplants.

There may be different degrees of plasticity depending upon the origins of the tissue and this is an area of active research we know. But to that extent some of the issues are the same. Where the issues tend to be distinctly different usually lies in the specific ethical dilemmas around the collection of the original material from which the derivation takes place.

And so you'll see it will go through the CIRM guidelines specific general rules sometimes about the (unintelligible) for example. I meant a specific set of special rules that govern speed of tissue collection, (unintelligible) collection, et cetera.

Next in section 100002 we have the absolute prohibitions of what CIRM will not fund and these actually track very closely with the National Academy's guidelines of the recommendations for what ought not be done. So here we find something very similar. Basically, we should not be doing reproductive cloning -- that was overdetermined by the California Proposition 71 measure

anyway -- culturing in-vitro, embryos, and here more specifically, the products of (unintelligible) parthogenesis and androgenesis for more than 12 days. You'll note 14 days is the more common international limits; 12 days comes from Prop 71.

The introduction of stem cell line into non-human climate; embryos that is - that has to do with a set of concerns about the developmental results of taking human and non-human stem cells - sorry, taking human stem cells and placing them into non-human primates where the species are so close that the actual way in which this would develop is a little bit difficult to understand as oppose to situations in which the tissues are so far apart with the organs, you know, particularly the order of systems, its later development, is so far away from something of concern that you don't really worry either of that animal welfare or the kind of intrinsic nature of the resulting entity. Here because it's introduced at the embryonic and because it's (unintelligible) it does (cause) a bit of a concern.

And then a provision on the introduction of stem cell from whatever kind of specie. This is (unintelligible) into human embryos because of the concern about the effects on any live born humans from such an embryo and the general concern about embryo manipulation when you have a reproductive outcome.

And finally, addressing what is everybody - from - everybody says in extremely remote risk or simply a risk that one did not take is a prohibition on breeding in animal into which (unintelligible) (central line) and that means human (central line) has been introduced against the remote risk that what you've got is an animal that actually now has human gametes as opposed to its own tissue gametes in it; remote but seemingly a simple enough kind of precaution.

Next is the requirement that there be the creation of one of these escrow committees. And here I want to note that it is -- and I'm going to skip the compliance section because it's really (unintelligible) administration. If you look at 100005, it is a committee that's made up of people with a variety of areas of expertise that is supposed to balance the scientific needs for an area of research with the ethical issues that it poses as well as provide a kind of record-keeping mechanism and facilitate education.

The - we call them SCROs or escrows without the E but still pronounced as escrow for convenience, thank you. The SCROs under the term regulations, if you look at them, don't look a lot different than an IRB but they're not an IRB. An IRB have their own missions of mandate.

So in the conversation - in the round up to the development of these regulations, there were many people - for example, UCLA was very active in these discussions, that talks at length about the value of allowing the IRB or a subcommittee of the IRB to take the lead in functioning as an SCRO in order to avoid the need to duplicate a committee.

The way these regulations are now written, there is some flexibility here in how one can construct an SCRO and have it interrelate with the IRB and it's something that you might want to pay attention to in an effort to figure out how to comply with the state law and the CIRM rules at the same time since many institutions, researches will be getting money from both or different laboratories will be getting money either from a private researcher and another laboratory from a CIRM researcher and a single institutional approach to review (and) record-keeping might be (why).

So I point out simply that it is not at all inconceivable, no pun intended, that you might be able to use much of your existing IRB membership to construct your SCRO or you might be able to create SCROs that's been - technically report to your IRBs so that your IRBs are able to technically comply with the legal requirements in your state law that governs non-CIRM funded research.

In 100006 we see basically the approach that CIRM is going to be taking in the question of the ethical standards it will have applied to the funded research. That is for new derivations, derivations being done with sole funding, you really need to have special justifications on why you need to derive a new line instead of working with an existing line since - while the regulations do not take the position at the destruction of an embryo is something that ought to be prohibited neither is it something that is viewed as being as unproblematic as the use of other kinds of human tissues.

For use of an existing line, for example a line that was already derived with CIRM funding or a line that was derived elsewhere that you would tend to import it to your laboratories, the requirement is that if you plan to use that existing line or imported line with CIRM funding, then the line has to meet a certain minimum set of requirements. These requirements represent a kind of core set of values that will be applied - whether it's CIRM-funded derivations or it is imported line, the same core set of principles are applied. And those core principles include - and you'll see this in 100007 that the donors gave voluntary and informed consent that there was no payment for the original tissue and that the donation was undertaken under the supervision of an IRB or its equivalent because in many countries they have a different (oversight) system.

Now we also knew that there are lines that were already approved to research with NIH fund that there lines that have been approved and licensed by the

UK Human Fertilization Embryology Authority and deposited in the UK stem cell bank or had been developed in accordance with the Canadian rule, all of which met these same core requirements and therefore, because we thought it was efficient as the social systems in which we had confidence, they were well-known, well-understood, well-documented, you will see in 100007 in the list of what are acceptable research materials (that you can) - an important use of your CIRM fund that cell lines that come from the NIH, from the UK Stem Cell Bank, from the Canadians, et cetera -- all automatically are considered acceptable.

And if they don't come from those places, they come from another country. France has just agreed to allow new lines to be developed from surplus embryos. If they come from France, you'd have to meet the core requirements that are laid out in 100070.

There is a new twist on that because just about two weeks ago, the United Kingdom has changed its position and now it's authorizing de minimus payments to egg donors. The payment is at this point, I believe, it was either 15 Pounds or 25 Pounds - 16 Pounds which is about $25. There is a discussion about moving it up to a maximum of about 250 Pounds which would be I think around $354.

That will then of course require that we think hard about this question of ethical relativism, ethical imperialism and trust in our compatriots in other countries with different systems. And this is why I mentioned in the introductions that I am - and this is also to remind you of the (conflict) working with the International Society of Stem Cell Research's bioethics body to come up with a set of recommendation for a kind of core set of ethical precept that would allow for essentially mutual recognition and use of one

another's materials and still feel like you were needing some set of core ethical standards.

When it comes to new derivations, the rules allow for us to get a whole lot pickier because there are new derivations, new people with the opportunity to take control of things that we can't control of - can't control, that's a place in the past. That's not to say that there is a judgment that everything that happened in the past was unethical. It is simply to say that within the universe of things that are unethical, unacceptable, there are also the different ways to do it and you can make adjustments and (unintelligible) your system and change your rules from here on out.

So 100008, additional requirements for CIRM-funded derivation. I think the most important thing to notice are that when you're talking about egg donation, in particular, that the CIRM regulations call for a promise of compensation or -- sorry -- promise to assume the cost of any medical care required as a direct result of the oocyte donation.

This is novel and it is not commonplace in the area of human (subject) research generally that such a promise be made; not even in things like Phase I research in the context of drug development where there is absolutely no possible benefit to the research subject where in fact the possible benefits of the research are few since most drugs fail to survive development from Phase I all the way to Phase III and approval and where the risks are at their most difficult to assess because the only data you have is in-vitro in animal data and you're dealing with healthy volunteers. Even there we do not, as a general process, guarantee an assumption of any medical cost that are a direct and proximate result.

This was included both because of consistent request from people - from the public who were commenting and also I think as a practical matter because it was doable. The risks of egg donation are actually fairly well-understood and they tend to manifest themselves within a reasonable period of time of the donation. In fact, to such a degree that there is already in the non-research, we've (unintelligible) an insurance market for short-term insurance policies specifically to cover medical care in case of adverse events associated with egg donation.

This is, I think, the (unintelligible) example of something where the CIRM regulation, they go further than you want to go in your state guidelines; it's up to you. This simply becomes a condition for receiving CIRM fund. It doesn't tell everybody how they have to do things.

One hundred thousand nine is form consent requirements. General and form consent requirements for all people donating all kinds of tissue that might be used in stem cell research emphasizes that the donors are perfectly entitled to register their preferences about what can and cannot be done with their - with the result of stem cell lines. And of course to make that real, we spell out in fairly detailed way the kinds of experiments you have to describe and also try to anticipate what would be a (unintelligible) issue.

To answer (unintelligible) on the record even though he is not here, the concern about telling people whether their eggs will be used in androgenesis - I mean parthenogenesis or an (sTnC) or fertilization came from a recognition that there are hot spots and topics for the public. Some people are opposed to genetic engineering. Some people oppose cloning but support other forms of embryonic stem cell research.

In an attempt to make the consent as truly informed as possible, we try to take the subjective point of view. That is, you ask what would the donor want to know rather than what's the reasonable researcher or professional thinks the donor (also) want to know. And therefore, we're trying to list those things the public and the donors would really want.

Having heard that information, they are free to say, you can use my materials with this but not that. Researchers of course are free to say, that's too complicated. I'd rather not accept the donation. I appreciate the offer. But no, thanks. Other researchers will choose to accept it and anybody who takes that line is expected then to abide by the specific preferences that are documented along with the line.

We will see over time how it works out. How many lines are given without much restriction; how many lines have restrictions that the researchers are unwilling to live with, we don't know.

For egg donation, we also have special rules about the kind of risk information that has to be given. I'd like to note that this is far more detailed than you would usually get in regulation. If for example the code of federal regulations (to) somebody to look at how the IRB has handled things and it says that the investigator shall explain the risk and benefit under, you know, as best as understood under current medical literature, et cetera.

Here I really think manifested as a kind of lack trust in the process an in the ability of the medical community to respond rapidly. There was an effort to identify those core concerns - core medical risks that absolutely has to be revealed and of course this is not an exclusive list. If a physician or an investigator or anybody else involved in the research learns of additional risk, the expectation is that these risks will be - this list will be supplemented

because the real goal is that people understand what they're doing before they say yes.

There are also some special rules here about cord blood donation in terms of who has to give consent. I'll let you pick up on that if you're interest in it later.

And finally, there is the goal that there'd be a kind of central repository of information so that institutions know what's going on at their institution. That would include non-human subject, non-animal, non-genetic engineering research. Just knowing what's going on in their laboratories. This is purely about public confidence.

This comes from the National Academy's guidelines and it does pose to some institutions a bit of a challenge in terms of the way in which they ordinarily manage their laboratories and their medical schools. Some of the information is already available through their (grant's) database but it may not be accessible in a way that we are recommending it be made acceptable here.

I've talked way long and happy to answer any specific questions you may have about the CIRM reg or the NAS guidelines.

Man: Thank you very much, Professor Charo.

Let me just - before recognizing (unintelligible) take some questions for Professor Charo then take a short break then Professor Magnus will talk in ways that I think will parallel some of what Alta has talked about, some gaps or some other issues that you think this committee might want to take up beyond - other than what CIRM has done. And then we'll decide what next steps to take, have public comments and adjourn (was) my expectation.

So questions from the committee for Professor Charo. Professor Weissman.

Irving Weissman: So while you were talking, I was just trying to think of a couple of particular instances that might need clarification. Maybe it's already there. So a number of people are thinking about alternative ways to produce egg that you could use then in experiment for nuclear transfer. One of them would be from a woman having an ovary removed incidentally with another surgery. So she's alive, days alive. But what concerns would this - what kinds of advice would you have for people saying to the (woman) this is part of your ovary and it might be used for this research. We can't guarantee its success. So I'll do that one first then I'll do a second one.

R. Alta Charo: Yeah. I think first of all or I think a lot of us are hoping that we learn how to efficiently mature eggs in-vitro so that we have a virtually limitless source coming from discarded surgical tissue from ovarian section.

Clearly, tissue donation is of concern to two distinctly different points of view. First from the physical risks associated with the donation and that's where the - today's egg donation which involve stimulation in order to get multiple eggs poses some challenge to some people. And the second has to do with privacy concerns when anybody is developing tissue that might be developed into a immortalized line by any means; whether it's done (unintelligible) in which the line itself now has information that either 100% or 50% depending on whether it's your gamete or your somatic cells that are being used, provides some information about you.

So I think it's important as the technology moves forward to always keep in mind the two sets of concerns, physical risk from the donation, privacy concern from the donation and to address your regulations accordingly. These

CIRM regulations were all developed with the model in mind of ovarian stimulation and then retrieval of eggs. They were not developed in mind with the in-vitro maturation of immature eggs.

Irving Weissman: Well the second question is almost the same question. For a number of medical research, objectives, sometimes the person who recently died has an autopsy done within two hours in the tissues obtained. But now the person is dead. He may have consented beforehand or the family member may have consented beforehand or under the anatomical gift actually to be used in the tissues. Anything else coming from that?

R. Alta Charo: Well this is going to be one - if this field moves toward collecting tissues, whether it's somatic or gamete from neomort, the recently dead. I think that's going to require - (unintelligible).

Man: Never heard. Neomort. It's the one thing I'm writing down.

R. Alta Charo: I'm glad I finally after an hour said something you didn't know already. I think that one is one where you might want to sit down and think very hard before jumping in with rules.

And the reason is this, right now human subject (rules) in the United States do not cover research on the dead. They cover only living individuals with the subjects of research and yet we know that research on the dead can in many cases be as ethically problematic as research on the living.

Research on the dead can be highly revealing of information about people who are currently living. Research on one person who's dead revealed a great deal of genetic information about his twin or probabilistic information about his near relatives. It also, to the extent, that we worry about our reputation

after death has reputational implications. We know that some people who do historical research and do retrospective medical diagnoses of historically important figures.

Despite this recognition, that it is not ethically unproblematic, a number of commissions including the bioethics commission under President Clinton shows not to tackle it because as soon as they got into it they realized what a mess it was because essentially it meant that any number of living individuals today would essentially have veto power over research on a particular dead person with multiple individuals all potentially being in conflict, some consenting and some refusing, just as relatives giving or refusing consent for one another's specification, in for example genetic research, raises similar problems.

I say all this only because getting tissue from the dead certainly deals with the problem of physical risk. It doesn't get rid of the problem of public sensibilities which sometimes are even more agitated when it comes to work with cadavers than work with living individuals. But most of all it becomes potentially a precedent to the entire field of human subject research and ought to be addressed with some attention to that potential implication.

Gregory Stock: Just also, if you would just comment briefly on the notion that it sounds very reasonable to have a major focus to be responding to public sensibilities, really, which are usually highly characteristic of an infinite time especially with new (source) of procedures of this sort.

If you also couple that with the important - the need to harmonize all sorts of diverse regulatory for the (regimes) and over time as well - it becomes very rigid and it becomes very hard to change those. So you almost invariably will end up to the situation where the regulatory structure was designed to respond

to the concerns that are possibly no longer even present in the public but it's not very, very difficult to do. There is - those concerns are very minority and (unintelligible) at this point.

So it seems to me - just your thoughts about that as opposed to the idea of creating a structure which you really feel is essentially justified by the dictates as we see them of the procedures that are involved and what we believe to be reasonable concerns in some way and use that to lead opinions on something.

R. Alta Charo: Greg, I have to answer this in my personal capacity now and make it very clear I'm not purporting to represent CIRM or the NAS committee in my view. Okay?

Personally, I think that there is a world of difference between the decision to criminalize something and the decision not to (send) it. So crimininalizing something, I think, requires that we actually hear some kind of philosophical logic about what is truly right and wrong and also reflect all of the other important values, constitutional (unintelligible) and political philosophy of values having to do with the role of government in regulating individual behavior and individual morality.

By contrast, when it comes to the question of what we will fund, I think there is much more room for making decisions based upon political pragmatism and the desire to not let the (best) become the enemy of the good, the desire to see groups genuinely come together in support of something because they now feel that their concerns have been addressed and therefore enhanced the kind of civility of the endeavor.

And to see whether or not within this more limited range of degrees of freedom within the funded world whether the core set of goals can be

accomplished before pushing on the edges. In other words to see whether or not you can see the (unintelligible) moving forward and move rapidly toward patient's therapeutic within what is absolutely acknowledged to be an unusually narrow set of rules or what you really need to liberalize certain things, whether it has to do with paying people or it has to do with the range of (unintelligible) you can do, et cetera.

And that latter set of judgment about exactly how rigid and narrow you can get in order to enhance civility and interchangeability, et cetera without compromising the research is a very impulsive judgment. And I completely accept that reasonable people can reasonably disagree on (unintelligible) those lines and to prognosticate about how the political world will respond to them. Right?

But that's what's going on. And in that sense, I think the CIRM regulations are more easily (unintelligible) than the NAS guidelines because like I said the NAS guidelines purports to tell people how they should go about doing their business; whereas the CIRM guidelines just say, this is what we'll put our money down on and this is what we won't. So in that sense I think the CIRM process was easier than the NAS process and the discussion about (unintelligible) as well.

Man: Two questions. First, in Section 100008 the - on the issue about paying for the medical cost, I just wasn't clear in looking at that and (unintelligible) also of having look at some other proposals for research where similar kinds of issues are applied to the wrong stem cell research address these issues. Most of them actually distinguish sort of cross over and above existing insurance that the subjects already have.

But I know that (unintelligible) is here so that - it's just that the institution must have paid for. So in situations where the research participants or the research donors rather in this case already have adequate coverage that their cost would be covered, this requires that you essentially bypass - using their already fully covered - as a way of doing that. That seems like an expense for the institution that seems unnecessary.

Am I misreading what (unintelligible) is?

R. Alta Charo: Those on the phone, you have got to understand Dr. Ahmad is very kind we're running back and forth with the one microphone here.

There actually was a discussion and you can look at the transcripts of the Los Angeles meeting last month on this point when the proposal was first raised and there was a discussion about whether the obligation here should be primary or secondary to existing coverage. And honestly, I don't believe we ever resolved this completely. We talked about it but I got the sense that it never got resolved. It certainly never got reflected in language. And I think it's a perfectly good area of a public comment in order to continue that discussion.

Man: This is just a follow up on Dr. (unintelligible) comment on the first requirement in that section for one is providing oocytes for research and clinical and fertility treatment which shall not compromise the (unintelligible) reproductive (unintelligible).

So I don't understand what that (says). So that's (unintelligible) and things that it can't be met. So I just want to know exactly what is (unintelligible) there. There's the idea that women are donating oocytes at the same time they're going (unintelligible) and clinical and fertility treatment at the same

time and so nothing is going to get undermined because the requirement is stronger than that because you're really saying that oocyte procurement shall not compromise optimal reproductive success that is something that cannot be (unintelligible) technologically.

So I just wanted to get clarity on that.

R. Alta Charo: First, I have to warn you that this provision came out of a discussion that took place in one of the CIRM meetings I was unable to attend and so I just want to note again that Geoff Lomax from CIRM is in the audience. He introduced himself earlier and I may ask him if he'd like to expand on my answer.

My understanding -- and it may not be clearly written enough -- of the intent of this provision was to ensure that while undergoing an infertility treatment that the donation of eggs not compromise that treatment.

For example, if a woman is producing egg for in-vitro fertilization for herself where we all know not all eggs will fertilize and not every cycle will result in a pregnancy so you tend to want to use all of your eggs, fertilizer as many as you can, store the extras, use a few at a time that's (peeling off) a few of the eggs that are produced at that time so research might be construed as having (unintelligible) optimal success; unless you have independently other reasons you want to limit the number of eggs that ever get fertilized. For example, some people don't want to store embryos for one reason or another.

It was not my understanding that this was saying that essentially we have to guarantee that egg donation can never in any fashion cause an adverse event that might possibly affect your fertility in any way in the future. But if it's not clearly written, it should be written differently.

Geoff, would you like to add anything here?

Geoffrey Lomax: Well (unintelligible) only to say that it's just the first characterization is correct. (Unintelligible) the record the (substance) of the discussion is really about the management of the donated egg and if there was a potential for donated eggs to be (unintelligible) in some way into the research pool prior to a woman's or a couple's ability to (reach) their fertility goals.

It was really focused on the management of eggs (unintelligible) again on that insurance issue the idea was that even individuals with insurance could be suffering economic loss in the event of (unintelligible) policy to cover cost (unintelligible). So that's again (unintelligible).

Man: (Unintelligible)

Geoffrey Lomax: Both (unintelligible) again that's (unintelligible). I'd be happy to (unintelligible).

R. Alta Charo: I think, you know, once the (unintelligible). I think one of the things that's extremely valuable about this committee's existence is that it offers you of an opportunity to think hard about places where you can tell already that your work may run into trouble if these regulations were adopted exactly as is and you can give your comments rapidly.

The logistical complication is that CIRM is already well into the administrative process when the common period opens which will be in the next couple of weeks. There will be a very short 45-day window in which to submit those comments. And yet once that window is closed and the regulations become finalized, in a sense this committee is to some extent

locked in to the CIRM regulations to the extent that one can say consistent with them.

So it does suggest the value of deciding among, you know, as we go through these comments, which ones are really worth pursuing rapidly to at least get into the (comment) period so that they become part of the discussion of how to amend CIRM reg.

Woman: I was wondering about the interaction of the prohibition on payment and the consent of donors for embryos that were already created. So for example, you can use blastocysts or embryos that were already created, I gather, for fertility purposes and presumably eggs could have been paid for in that process so long as the consent, I guess, of all the donors is obtained; presumably including the people who donate - who "donated" who were paid for their eggs. And that would not violate, I believe, but I was trying to read this altogether the prohibition - because the prohibition upon payment applies only to embryos that were specifically created for research purposes. Is that correct?

R. Alta Charo: If you look at Section 100007, Acceptable Research Materials and you look under Subsection E, right? Because Subsections A through D list all the other kind of established licensing and approval programs that we are simply recognizing as they kind of form a national mutual respect.

Under E you see that cell central lines were derived under the following conditions and now we lay them out that one, the donors, they voluntarily (unintelligible) consent and two, the donors did not receive valuable consideration.

That I understand from the conversation at the table means that an embryo that is being donated by a couple who has themselves paid somebody for eggs or sperm is not usable, not usable; that the lines from such an embryo cannot be used. This has posed another challenge to people because in some cases it's not clear that the existing record-keeping is good enough to be confident about the underlying condition by which an embryo was created all we know is about the people who are actually doing the donation.

I understand that this is also an issue with regard to the National Academy recommendation because it also said consent in the future from embryo donation in which consent should be obtained from all the progenitors as well as in sense the legal custodians of an embryo. And that means that embryos made with donor sperm and donor egg should not be used unless those original donors can be tracked down and consented.

Again, I think a perfect example of what Dr. (Unintelligible) was pointing to as a substantial narrowing in the name of trying to peel off areas of controversy and see if you are still left with a work of a population of materials without having to tread right on the line of ethical controversy. And in the area of dummy donations for the underlying embryos, it was our understanding at the National Academy that approximately 10% to 15% of the embryos out there would no longer be usable for the development of some cell lines.

That seem to be a manageable reduction in the universe of available embryos in exchange for avoiding what could be a very difficult debate about whether or not donors who originally thought they were helping a couple to make a child have somehow been wronged even if they don't know they've been wronged when their materials have now been diverted after a failed effort to

help a couple make a child into an entirely different enterprise which is trying to help save somebody's life.

The very interesting debate that has a bit of angels on a pin quality to it but there's also some value to avoiding it if in the end we can still do the research with the remaining 80 to (unintelligible).

Man: (Unintelligible) probably useful now for people as well as other physiological functions that need to be attended to. Let's break for 10 minutes. Come back at 3:20.

David Magnus: …a limiting factor; whereas my understanding of what our chart is having talked to Dr. Shabbir about it and when you look at the (SB 322), we are coming up with guidance for IRB. So one of the things that might be helpful in ways in which these things can work together and I've got a few areas of suggestion but I'd stressed that (Alsa) and Bernie probably have some other ideas, areas where they think it might be helpful to have guidelines rather than regulation that could supplement the regulators concerned so that we get something that we'd be able to fit together very well.

I think the issue o the - I didn't put this in the presentation but one example that is - the interpretation of the requirement of the regulations about payment for the medical care where that's seen as somewhat ambiguous which is arguably might be, we can come - strut some guidance for IRB which would offer interpretation of that and I can sense that it's been very helpful.

So most of what I'm going to talk about has to do with those things.

The second thing though - area is to begin, I'm going to give a couple of examples but I think we should start to begin to think about what happens

when we actually get to the point where we're going to be doing clinical trials for human embryonic stem cell research and my understanding is that in the private sector that time is actually possibly now that there are maybe some human embryonic stem cells clinical trials that are going to be taking place very soon.

Given that fact, it's a little bit consorting that the (unintelligible) report and the guideline have focused almost exclusively which (unintelligible) on the issue of procurement of oocytes; but going forward, there are a lot of issues that we have to deal with these clinical trials but so far there's really been not much done.

Just a trivial example that I'll get to later, everyone correctly pointed out how important it is that we have consent from all (unintelligible) donors because they may not approve of stem cell which given its sensitive nature is appropriate that we would require (an absolute) informed consent to understand what it means when they're donating this material. But surely the same thing is also true of recipient of material.

So for people who are going to have tissues put into them that are derived from destroyed embryos, that should probably be included in the informed consent process but that's not in any of the guidelines.

Woman: It's already required by the FDA.

David Magnus: That you've got them the informed consent process that you point out that - as destruction of embryos (made) they require for the procurement…

Woman: No, no, no. The informed consent for recipients - required by the FDA regulators.

David Magnus: Yeah, but…

((Crosstalk))

David Magnus: …particular content of the consent. Everyone has said that for oocyte donors, it's really important that the content of those consents should be aware of these very sensitive issues. That's also presumably true if the people are going to be recipients of the tissue. So far that's not (unintelligible) in any of guidelines or regulations.

Again, I talked to (John Marino), who is co-chair of that committee; when they were working on it, he just said, they decided that that's not going to - I mean, they're going to deal with that down the road. And it maybe that (unintelligible) funds clinical trials would only be funding its early research in which case wouldn't apply, the procedure is going to take place when it's appropriate for the state guidelines to absolutely give guidance on what's going to happen the next steps of clinical trials.

So, let's go ahead.

The first thing I want to talk about is something that (Michelle) and I talked about in our (unintelligible) and science which is how we think about donation of oocytes for research purposes. In cases where people are donating excess IVF embryos, we have a really good understanding of that process and (unintelligible) that.

We have a clinical consent for the procedure to produce procure oocytes, (something's) going in for IVF, we understand that, their risks, there's talks about that; they weigh risks and benefits, they make a decision, they decide to

donate some excess IVF embryos. There's a research consent for the use of biological materials along with some of the other issues that are in the (certain) guidelines of - guidelines.

And then when we get to clinical trials (unintelligible) consent are understood. But what do we do about non-medical oocyte donors? When oocytes - when women are donating oocytes just for research purposes, they're not going in for reproduction purposes. And when we first start thinking about this, when you look at the federal regulation, this tells you how bizarre this situation is.

If the material is untraceable to the researchers and the people who are procuring the oocytes are not themselves investigators, then the people who are doing the research are investigators under the regulation but not doing - arguably, not doing (human subjects) research.

The physicians who procure the oocytes are not investigators but maybe doing (human subjects) research. And this is - prescribe the meds, (unintelligible) the donor is neither investigator nor doing (human subjects) research and we try to figure out what the nature of the relationships of the donor is, are they the physician - is this a patient-physician relationship, are they researchers. It's hard to figure out exactly what the nature of that relationship is. And so what is the donor status in relation to that is kind of tricky.

So - and this is important because donate - (unintelligible) are significant risks to being an oocyte donor, ovarian hyperstimulation syndrome, ovarian (portion), hospitalization is not uncommon, renal failure, infertility, and even very rarely, death.

And this is - (unintelligible) important is the goal of the oocytes that are procured is going to be for (unintelligible) transfer. Because there's at least

some evidence that you're going to get better results if you get the donations from very young donors, although I'm not sure of the status of that evidences right now because a lot of that is based now (this credited) work from (unintelligible) and the team in South Korea. Ovarian hyperstimulation syndrome is more likely in young donors and if this does turn out to be true, then this is going to be an even greater problem for the women who are likely to be oocyte donors.

And I'll just point out that partly as results of these two factors, in South Korea, of the first 100 donors, 16 developed ovarian hyperstimulation syndrome that was actually fairly serious, and two wound up requiring extensive hospitalization as a result of the side effect, as a result of their donation.

So, how do we think about this? Should this be thought as the clinical consent? Well, not really, because the donor is not a patient and if you really think about those risks for these women but no benefits for them except really think of the (fiduciary) obligation (which is not) they don't do it. On the other hand just thinking of it as a research consent is problematic because I don't think it captures the nature of the interaction properly.

Moreover, I would think we argue that there is a risk that you may focus on the research aspect of the donation process which is - to an extent which you are a tissue donor rather than on the well-understood but not experimental risk of being an oocyte donor.

One way of doing that is the way that the (certain) guidelines have done that by really just (unintelligible) that you may have to make sure that you cover these things adequately but we're worried that regardless of what's in the informed consent process, it's likely that that's - that may not get covered in

the actual discussions that take place and that (unintelligible) borne out by what happened in South Korea.

So we suggested that there should be a new category of research participants in addition to subject, you know, the women who are donating these oocytes for research aren't really research subjects, that doesn't really capture what it is that their roles in this process and we could just (unintelligible) research donor; they're distinct from subjects, they're also distinct from other kinds of donors with biological material where - like sperm and genetic material where the risks of procurement are minimal.

And to make an analogy, (while) organ donation just had similar sort of conceptual issues about figuring out what the nature of their role is with respect to (position) and that we should take the lessons from that of close (unintelligible) donors, make sure that there's adequate psychological screening, serious weighing of benefits - of risks versus benefits, weighing of this kind of procurement process.

And so I think it would make sense in thinking about guidance to IRB that they really should recognize this as a distinct category of research participants and that people should conceptualize research in this way. I think that will do a much better job of capturing the relationships properly.

Another thing that we've just found from looking at consent forms, including (thinking true) for ourselves, worry about, just sort of an example, some kind of areas where confusions may arise and where we might be able to give guidance to IRB to help avoid this.

What it means, for example, to be identified versus anonymized. And when we've looked at consent forms, it seems often that researchers inadvertently

use the wrong language with things that they thought were anonymized just be identified and this could have absolute implications for what the consent process should look like.

IRB should know the difference between these two but researchers often don't and so I think we should recommend that researchers be educated about the difference between these two as we go forward.

Next, Bernie Lo and his group published a paper recently in which (PR) did something that - also have been telling us for over a year but none of us wanted to hear which is that because of FDA requirements about - that are going to be in place before putting tissues into bodies, these are some of the comments you made earlier, realistically for all of the different kinds of reason she already talked about with many of these, is likely that we are going to have to do follow-up testing for the donors of materials before we're going to be allowed to put any materials derived from stem cells in to people's body.

And this means the paradigm that we've been using for thinking about this, this sort of genetic storage where we create as many firewalls as possible and try to anonymized it as much as possible, probably isn't going to work as we go forward if you want to use any material.

Now, that is - again, we get some of that guidance but not a regulation. It seems that this is something that you want to put in there so that IRB can make sure that researchers are informed that if they've anonymized the material, if they haven't put anything in place for re-contacting donors, the researchers need to understand that that means that the tissue they derived from that are probably not going to be things that they're going to ever be able use.

And so, that may put some things that would be appropriate for making sure that researchers are knowingly making decisions as they go forward with that.

We made sure that certainly our people at Stanford know that as they go forward but I think it's important that we make sure that this happens for all researchers, we don't want this to have a situation where down the road somebody derived some materials that four or five years later looks really promising for clinical trials but because they didn't set up the consent process and the re-contacting process in the right way, they can't use that material. That would be a real problem.

That raises the issues that Bernie Lo also talked on the article that we're going to have to make sure that we do a really good job at confidentiality. I have no copy recommendations here. But if we're going to re-contact people, that way we've - the paradigm for confidentiality is very easy when we think of this as the genetic storage model and just create a lot of firewall.

We understand how to handle confidentiality very well that way. But if we're going to have re-contacting, I think, we don't really have a good system in place or thought through what it's going to take to really maintain confidentiality under those kinds of circumstances.

Given this a very private decision and that the stigma or words of political (unintelligible) that might result in that knowledge becoming public is very real. You could easily imagine if we send letters, you know, to people to their homes to tell them that we need them to come in to be re-contacted and they've moved, the information could fall into somebody's hands and the last thing anybody wants is protest and showing up to somebody's house because they donated excess IVF embryos for stem cell research.

So we've got to have some ways of dealing with privacy rights; unfortunately, (unintelligible) recommend this is a huge area for problem, it didn't say much about how to solve it and I don't have any idea of it either but I think we really need to think hard about exactly what that's going to look like, frustrations we're going - constantly will be in contact with people.

Also along with that, we're going to stay in touch with people and do retesting, we have to recognize that there's going to be potential for (internal) findings. And we might get results that could have health implications for those people and that means now when people donate their material, we need to warn them that that could happen and figure out how we're going to deal with that.

We need standards for what and how, (medicals) to make sure are going to be communicated to those donors and we need to build that into the informed consent process now. And, again, that's going to be some of the challenge but I think some of those are important that we work out now.

Other consent language problems. So this one - something that we certainly found was an issue that we were worried about locally, I'm not sure if this is true everywhere, but one thing looking at those different consent forms from different institutions, the meaning of excess embryos was very vague between excess from this particular (attempted) transfer of embryos and excess from (attempted) having a child.

And the worry here is because we often thought consent forms that both cover the use of sub-par embryos for immediate use and the use of later of excess embryos, the worry is that researchers may wind up using embryos, the couple want to go back to if the current (attempted) pregnancy fails and there are

other embryos that are of high enough quality so you may go back and find those things and find that they've been destroyed for research purposes.

Similar kinds of concerns are clearly embodied in the term guidelines or concerns about taking extra oocytes but I think the same things to worry even when it has to do with the use of embryos so we recommended that we - that you actually distinguish that two separate informed consent forms, one for dealing with the donation of sub-par embryos sort of for fresh use and have that a different consent process than the process we're using embryos that are used in storage to just avoid any lack of clarity that clearly be in a lot of consent documents and that's how we've been dealing with that problem.

Another problem, the therapy's misconception, and this is just the lessons I think we should learn from our experiences with gene transfer research. Obviously, gene therapy had a lot of hype, desperate patients, (unintelligible) researchers and resulted in a lot of misleading language and a lot of them written about the therapeutic misconception. I'm going to give you a couple of examples and even calling it gene therapy.

You know, most people (writing about), this is a problem, there is no gene therapy, nothing has gone through Phase 3 successfully, we shouldn't call it that, we should call it gene transfer research. I think a very similar situation could take place, and it is taking place, human embryonic stem cell research, a lot of hype, desperation, enthusiasm.

So one recommendation that I think we should have is that the new term, therapeutic cloning at the present time should not be present in any informed consent form. There's no such thing as therapeutic cloning; it doesn't exists, so - at least not at the present time. Maybe someday there will but there isn't

now and so we shouldn't call it that and we should actually say that that's not the language we should be using in any informed consent document.

So, just say a few words about going forward to clinical trials; I've already said I think we should think about that some more. There's only two examples or three examples that I'm going to talk about, therapeutic misconception, again, and treat the patient populations for initial clinical trial.

For - again, stressing, I don't want to avoid this, the therapeutic misconception already exist now with regards to oocytes procurement. So I want to make sure that we don't talk about therapeutic cloning in the oocytes procurement or embryo procurement process; (that's only what) we can deal with right now. But I think it's even more important when we go to actual clinical trials that we'd be very sensitive to the issue of therapeutic misconception.

And we know that we've done a poor job in the human - in human gene transfer research. This is a couple of examples from some studies of informed consent forms in gene transfer research. If you look at the different studies, they found misleading language used a very, very high percentage of the time; this just gives you a sense of some of these examples.

In this study, it's (unintelligible) to treat your disease by delivery of (unintelligible) organ. And even likely to be in research study of a treatment design that may help your immune system fight cancer, this study is designed to treat cancer patients.

They can understand why people who are under the impression that there's something that's designed to help them rather than something that's designed to learn more, especially given that in reality, most of what we get out of these things is learning about surrogate end points that we acknowledge for rather

than anything that's likely to have any actual, you know, therapeutic modality for individual patients.

Another example from (unintelligible), gene therapy works by using (ovarian vectors) that carry the new gene into the patient's cells and once there, the new gene, they could (unintelligible) the investigators hope that gene therapy be an effective treatment for your disease; again, these are from the consent forms that gotten IRB approval.

The hope is that we can improve your systems to prolong your life is the treatment. The purpose of this study is to determine whether this procedure is safe and survives effective treatment on your disease. So that's from an introductory section of an informed consent form.

Later, in the benefit section, they give a concept of (unintelligible), it is not possible to predict whether or not any personal benefit results. You put those two things together and of course likely the people are going to have a misunderstanding about what the point of the research is.

So I think we just want to do something to make sure that we give some guidance to try and avoid those kinds of problems. It would be nice if we don't have just a replay of all the problems that (unintelligible) gene therapy in the past decades, it would be nice if we could avoid some of those in human embryonic stem cell research.

Finally, on (unintelligible) population on whether human embryonic stem cell trials should be done on children. The four different possible findings that will allow you to do research on children includes that it's minimal risk, that it's a minor increase over minimal risk, but yields knowledge about (unintelligible) condition.

For most early Phase 1 research is going to be launched, it's not going to meet either of these two requirements; so clearly, it's going to have to be under - we just likely appeal to the fact that they might offer a process with a direct benefit to subject.

Another possibility of a finding would be if there's a claim that there's an understanding to help or treat disease that affects children, it's possible that Health and Human Services can create a committee with (unintelligible) representative that would approve a trial even if it fails to meet any of these three of these three.

So, is - so one question I think we have to ask and the IRB should be looking at really hard is when is there a prospect of direct benefit and what's going to be required.

Do we need proof of concept in human adult? The early human embryonic stem cell trials, the first time we do this, I'm worried that we may find, again, a repeatable result in human gene transfer trial where we have a concept in principle with animals but no - none use of primates but no real sign of these things work effectively clinically in primates so we will require first that we have some tests in human adults before we go to children and can claim a prospect of direct benefit.

Do we require proof of the concept in non-human primates or is (mouse data) plus sort of the other pieces of the story that you kind of put together typically in a gene transfer trial sufficient to allow us to go forward in these cases.

Gene transfer research or an awful lot of these clinical trials are really in the surrogate end points which are beneficial to research but have no clinical

benefit for the subject. I think, again, we want to avoid that situation in research on children for early human embryonic stem cell research trial. And so the one - the question is that we might want to ask is what kind of evidence do we need before IRB should be able to say for a (unintelligible) area like this that there is a prospect of direct benefit.

And then I already mentioned this that because it involves destruction of embryos, (unintelligible) trials material that we should in the informed consent clinical trials which should be include, you know, where these things come from and that it might involved the destruction of embryos.

Summary; recognized (unintelligible) category, clarified meaning, advice on the need to re-contact, advice on confidentiality -- this one's going to be really hard; somebody needs to think of some good ideas about how that's going to take place -- (unintelligible) on destruction of embryos stored for future use. Avoid the term therapeutic cloning. Avoid therapeutic misconception and consent and advice on (primates) clinical trials.

I suspect when we think about clinical trials in more detail we might come up with other things that would be good guidance that should guide researchers but this is at least a starting point, starting to think about some of those issues.

Man: So, let's take some time for any specific questions for David and then we'll move to a discussion of this committee's next steps.

Is there anybody who can put the lights on?

Dr. Weissman.

Irving Weissman: So, David, just as to bring up some topic, in many of the human stem cell research whether it's adult, fetal, or from embryonic, you're able to do a proof of concept in an animal model that's highly immuno-deficient but you're unable to do a proof of concept in a primate.

So, should you then not go forward with the clinical trial?

David Magnus: No, this is - the question - these are obviously really technical issues that depend on the details of the science.

For lots of clinical trials, I mean for adult stem trials, in hematopoietic research where you've got proof of concept in adults for at least some kinds of hematopoietic stem cell therapy, you know, (unintelligible) BMTs for a long time, you – I would say you already have that.

The question is, when you go into what I would call frontier research, something that really radically different from anything that we – that gone before, the question is, to what extent does skid mouse research really tell us about how successful it's going to be especially given that, you know, the people – you might do – give some immunosuppression to them, but that's not (unintelligible) say, but that's really not the same – doesn't have the same effect.

So the question is, how much evidence – I (unintelligible) into the question not an answer, but I think it's a legitimate thing to ask, how much evidence do we really want before we can say, there's evidence of benefit – to be able to claim that there's a prospect, a direct benefit for the intervention under investigation.

Some of the stories that get told for some gene transfer research, look kind of (menky), when you put them together. They, you know, they – we know there's lots of things that work great in mice, but it's going to establish pretty well that they don't transfer very well to humans and yet, you know, there's sort of pieces that you just have to put in place to be able to be allowed to go forward.

So lots going to depend on the details of that, but I think it's an open question whether or not for the first human embryonic stem cell trial, should those – and the first success, should those come with adults before – for anything before we allow the idea of doing any of this for children.

Man: Is (menky) a term of (art and) philosophy?

Man: Rather than establish a set of hard rules going forward that take care of large patient populations like children or like – you had to do primary (unintelligible).

I would just argue you need to go to it on a case-by-case basis.

There are many diseases limited to children, have no models in primates where you're going to have to take a chance if you have a therapy that for various good reasons, not mouse-to-mouse but human-to-mouse tells you that it works.

And I just want to make sure that we don't get stuck into a hard philosophical point of view and we really to do a case-by-case understanding what's going on.

Man: And one other thing (unintelligible) don't find there's not a positive direct benefit, doesn't mean that the research couldn't go forward. So you could give guidance for IRBs that would say, look we don't think unless you meet these conditions that you can do a finding under this category.

But that's another way of saying that for those categories of research, that they really ought to do is find it under that fourth category, that we're really saying is, if you haven't got proof of concept in primates or adults, for that kind of research, given how sensitive it is, given that – this nature it would be better under those circumstances to use that fourth category of having a committee look – (unintelligible) committee look and do the finding under – on that basis.

So I think that that would be better to do in cases where you're not sure.

So I think having a rule that says, you know, again just to be clear, it's not saying you can't do the research, it's just saying you can't use it under that finding.

Man: Other questions (unintelligible)?

Well then let me suggest a way that seems to me might make sense for us to move forward.

We have I think heard a lot of good things about the CIRM guidelines – CIRM regulations or proposed regulations. And we've also had some things that came up both in response – both in and in response to Professor (Charles) comments and then Professor Magnus comments about ways in which our committee with our particular charge might want to deviate from the CIRM regulations in our guidelines.

I don't think that we're going to be able to hammer out a position on that right now this afternoon in this meeting, with the relatively – with a quorum, but only a bare quorum of the committee present.

So, I suggest one way we might be able to proceed is to take advantage of the by-laws, provisions that we can appoint working groups or sub-committees or other bodies to advice this committee and have a working group from this committee -- members of the committee and fundamentally any member of the committee who wants to be on that working group, to think about the issues that have come up today and to report back to this committee at our next meeting with some pros and cons about making changes from the CIRM regulations, taking at least, I think, as a baseline, those CIRM regulations, and see if there are ways in which we want to deviate from them.

Example might be this issue of payment for (oocyte) donors. That working group or subcommittee may come back with a recommendation, it may just come back, saying here's the discussion we've had one way or the other, the decision ultimately would be in a public meeting by this state committee on what recommendations, what guidelines we would recommend to the department, but I think we would make much more progress if we had a smaller group communicating probably, heavily via email with each other and perhaps with the committee as a whole, to come up with some specific ideas and discussion on these topics which the whole committee would then take up.

That's a (unintelligible).

Woman: (Unintelligible).

Man: Yes

Woman: (Unintelligible).

What exactly would be the enforcement mechanism for the guidelines were they to be adopted. This kind of gets back to the issue that also raised earlier about criminalization versus non-funding.

(Serum) regulations clearly applied to (serum) funded research.

Are guidelines – the staff too doesn't say anything, so far as I can see about this. It simply says that, you know, the department shall establish a committee which will advise on guidelines.

Are guidelines to be enforced – are we creating regulations that would be criminal prohibitions or professional, you know, kinds of compliance requirements or what? What would really be the impact of our guidelines?

Man: I think one thing the subcommittee should recommend is a better technology for the telethon conference situation.

You know that's a great question (Monica). All I have just as all any of us have is just the text of the statute itself passed almost three years ago.

As I read this, there certainly wouldn't be any criminal liability for violating these guidelines. The fact that they're called guidelines rather than regulations makes me think that they're intended to be something other than regulation.

The fact that this statute is after so created, proposed by the same Senator who proposed SB 253 requiring IRB approval, makes me think it would be logical to view these as guidelines to help guide IRBs in their determination and presumably also could be useful for other entities like either the escrows or the escrows…

Woman: Uh-huh.

Man: …depending on whether you're using the National Academy's spelling or the CIRM's spelling.

But I, you know, all I know is what the statute says, I think that these are guidance for IRBs and others and do not have liability attached to them. It also however, worth noting that this committee and in fact the guidelines themselves presumably, it looks like, the guidelines (unintelligible) on January 1 of 2007, which is not very far away, at least everything about this statue (unintelligible).

It is possible, I think there's a good chance that somehow this will be extended by subsequent legislation, that legislation might also change what substance these guidelines are supposed to have.

But right now based on SB 322, the one we've got in front of us, looks to me that these are advisory guidelines for use by anybody who would have occasion to use them, presumably, primarily IRBs and escrows.

Man: So great stock.

If I'm getting this clear, these are guidelines which seem to me is fundamental to – in writing them to, or thinking about them at least for me, to understand in

what context they would be applied because my recommendations would certainly change depending on that.

And if in fact they – I realize that the committee was sun-setting, but it's the guidelines themselves are sun-setting at the same time, essentially immediately following their submission, that – seems a great deal (unintelligible).

So if – it would be interesting to me if anybody else has any comments about those two points, because another aspect is that the area that these were first were applied to, given the various exceptions that were described earlier rather limited, means that if they were the issues of harmonization and such, you might be able to use these to say, "Here is what we would consider to be – we can make a statement with such guidelines if you wish to.

I mean there are a bunch of ways of doing this and I don't have a very – it's difficult for me to think how to approach it, if maybe some other committee members who have more familiarity of the process could make some suggestions because…

Man: I'm at a loss here.

Man: You know, I suppose I may have misspoken to some extent in talking about the sun-setting, although it's not clear you could say I did.

The section that requires a little bit of guideline, sunset as of January of 2007.

Now guidelines that are out there that are published, they don't mysteriously disappear on January of 2007 and – the extent that they only have advisory recommendation – recommended (unintelligible)…

Man: Uh-huh.

Man: …to the extent that they don't have the force of law but are merely recommendations, they remain presumably merely recommendations even after the section that created them has disappeared.

I do think that if they were supposed to have force of law, which is not my interpretation of the statute, but that's your interpretation under California legislation, it’s not my specialty.

If they were intended to have force of law I think that force of law would disappear on January 1, 2007, with the sunset provision, unless it is extended, which I suspect it may well be.

It seems that the recommend – the power of the recommendation, the power of guidance or whatever power that may have, will likely extend beyond January 1 of 2007.

And I think what we’re doing is worthwhile despite that sunset date, but I don't think what we’re doing, is my interpretation of the statutes that what we’re doing is not a criminal statute, a regulation or something else that has the force of law.

Anyone else is certainly welcome to take a look at the statute and give it their own interpretation.

Man: But (unintelligible) if I'm wrong, (unintelligible) that neither were the National Academy of Science recommendation that these were basically statements that research done should comply with these guidelines.

And so it is a very strong statement. It's a – it's very different than saying, we will only fund the research that complies with these guidelines, though it seems to me that, you know, the idea that it is a force of law that's a different process, but certainly the intent is to say that research has complied with it.

Man: You know, actually I asked to amend what I said earlier, looking down here to Section 4 of the statute, which does require all (AGSC), all human-embryonic (SIMTA) research, all research projects involving the (degradation) or use of shall be reviewed and approved by an IRB.

Any such IRB shall in its review of such research, consider and apply these guidelines, which does imply that the IRBs at least through January 1 of 2007 has to take into account and apply our guidelines. What's the sanction if they don't isn't clear here.

It's not off with the heads of the IRB, but they are told that they have apply these guidelines.

So the guidelines have a little more force than I said a moment ago. At least through January 1 of 2007.

But there is no enforcement provision with respect to the IRB.

The IRB has to make reports to the department on (SIMSA) research project it has reviewed and approved. And the department has to report that back to the Governor I guess -- to the legislature.

So to get back to the suggestion I made for how to proceed, does anybody have – bearing in mind that he exact force of what we're promulgating is not

entirely clear between – for the next ten months, let alone after the next ten months.

Any thoughts on that method of proceeding?

(Bert)?

(Bert): (Unintelligible).

So I think the idea of subcommittees is worthwhile and we should proceed with that.

I guess the question would be, what would be the subcommittee – how would we divide up and what particular area? So there are different areas (unintelligible), subcommittee do the whole thing or would there be areas on particular, you know, differences?

One of the things that I was struck by what you said David is, that this could be partnerships between practices through (IDS) that are not in universities, with the universities, I would suspect.

That certainly might be the case in the (East Bay), with Berkeley and with us.

So where does that be? In the hospital where those practices are, may not even have an IRB or they might have an IRB who works at UC Berkeley's IRB says, "We don't even understand (it) during the year. We want to write a different one."

And I think the idea of trying to help set-up something, that helps foster the research and protect the subject is a good charge for us to have for this date.

So – but that's a different question maybe than some of the other questions.

So, I'd like to – our next meeting not to be, well now let's see what we should split off more or how do we think about in a comprehensive way so that we've covered as many of the bases as we can with (unintelligible) committee?

(Unintelligible), but I would move that the Chair and the Vice-Chair, in consultations when necessary, with other members of this panel devise subcommittees around subjects that will be relevant for the next agenda, find a way for them to work with and without committee members, and then come back to us.

That's my motion.

Man: (Unintelligible).

Man: We can discuss after the second (unintelligible).

Man: (Unintelligible).

Man: I would – although I did not plant this as my friend and neighbor, Dr. Weissman.

I do think that it could – it would be better to take some time and think about how many committees we need, survey via email and otherwise members of the committee to see who wants to be on which subject, to take some more time than we have today and – involving some more members of the committee than we have today in terms of figuring out how best to carve these subjects up.

But I would stress the intent of my idea, is not to have subcommittees come up with the answers, but to have subcommittees, working groups, etcetera, come back to the committee with suggestions, ideas, thoughts, discussion which the committee then will come up with the answers.

So, I genuinely do not anticipate or want this to be a situation where the real work gets done by the subcommittees, the real work will ultimately have to be done by us in public.

Dr. (Sap)?

(Sap): I would like to – if you go forward with that, I would like to suggest that probably a lot of people have read the various guidelines have some thoughts about, at least for particular sections and that a way of facilitating that for you would be if people would just send in what comments they have based on the discussions of today and any previous that they've done.

And then you could sort of formulate some provision or breakup and get further comments.

Man: Uh-huh.

(Sap): It would be a way of making – rather than being on a committee to try and organize the whole thing, sounds like a great deal as opposed – and it's uncertain how big it really is.

Man: Well, assuming (unintelligible) to keep my Co-Chair, (Bert) on the hook here…

Man: Yes.

Man: …I think that's an excellent idea and I would certainly hope that all committee members including those listening on the phone would suggest to us the topic where you think we might want to consider, differing from the CIRM regulation.

Other comments on this motion? On the discussion on the motion that is on the floor?

Anybody on – any of the committee members on telephone want to throw anything in? If you're there.

Man: (Unintelligible).

Hank Greeley: Is - (Elizabeth), (Rusty) are you still there? Anybody there?

(Margaret): I'm here Hank. It's (Margaret).

Hank Greeley: Hi, (Margaret). I didn't even know you were here at all. Welcome.

(Margaret): (Unintelligible) in on.

Hank Greeley: Okay.

Seeing no further discussion and hearing no further discussion, the motion comes to a vote. The motion is to vest in the Chair and Vice-Chair the discretion to suggest and create subcommittees or working groups on various topics, then move in second all in favor, signified by saying, aye.

Man: Aye.

Woman: Aye.

Hank Greeley: Opposed, nay. Any abstention?

Motion passes.

Are there – we also have on the agenda provision for public comment period. Are there other things that committee members want to say, other business you think we should take up or other comments you think we should share before we move to the public comment item on the agenda?

Again, seeing and hearing none, let me invite members of the public, first those who are here physically present, to ask if any of you have any comments you want to make to the committee?

Yes, ma'am please come up and (unintelligible) to the telephone.

And identify yourself (unintelligible).

(Cara Conference): Yes, my name is (Cara Conference) from – with Berkeley and at the time when this was (Cunningham)'s committee I was on it, so I'm going to talk about the issues that I was going to bring to the table, I think under that guise.

But there's a - particularly comments from the donor egg – the egg donor community. S a couple I'm going to go through some of which are very small points and some of which leads to logic guidelines.

One point from people undergoing ovarian hyperstimulation and egg – for examination and fertility treatment is that consent for this position of very dramatically or changes dramatically when you know the fertility outcome compared to when you don't.

So timing of consenting is very important.

The next point I wanted to make is one that's come up to me from a donor. Can I -- she says – agree with my contracts that I will be paid for all my eggs or the first ten whichever is less and if there are any over ten, give them for research?

So can I give extra eggs while receiving payment for the ones that I kind of contract the facility treatment? And quite a few people liked that idea. They liked the idea of doing that.

And get very worried about having lots of leftover embryos with egg and it might be used for other purposes on – in fertility clinics.

Another – a really major concern among the donor egg and the ovarian hyperstimulation committee is long-term effect. And I think that’s not addressed in the CIRM’s guidelines at all.

But all sort of reasons, the pathway that I would most like to see proceed is the people – that it actually set up as a scientific goal that in-vitro maturation of immature oocytes be pursued and ovarian section be pursued so that there’ll be money given to scientific – to clinical research in that area, that the research is already there for cancer patients per ovarian section and detecting (unintelligible) be bought to bear on this question.

And that there'd be some suggestion that would be preferred essentially even if we do some other – use some other oocytes retrieval procedures in the meantime.

Yeah, so the three concerns around long-term effects are, facility; that can easily be got around only – allowing women to be donors who have had their children or do not want to have children, unless (unintelligible) donors.

Any effects on children born after users undergone ovarian hyperstimulation, there's some evidence that there might be long-term effects in children born from (IVS), would there be – would those hold-up and are they also true for children born to women subsequent to donation if they undergo ovarian hyperstimulation.

And then ovarian cancer is a really major concern among the donor community.

So – on top of the scientific advantages to freezing ovarian tissue which are that you – that researchers can have – get many more eggs (per fry) and that they can thaw them when they need them, when they're ready to derive lines and give the research in question.

Okay.

And that last point, the scientific kinds, the science and ethics together I think is a general principle is extremely – would be extremely important. A lot of concerns among the – I do a lot of interviewing and me meeting with grassroots people around these issues.

A lot of their concerns are what, well, do scientists know stuff that's going to affect us later? For example, all these articles that are coming out about cancer being cause by stem cells, if you derive –if you begin differentiate from a stem cell line, in a particular direction, are there still stem cell lines there and if you deliver those cells, the cancer is going to grow where you deliver those cells, how do we know that's not going to happen?

So think that there'd be some mechanism put in place to have concerns come up in the science, that they go back to public and that the ethics not (rigidify), as you were commenting on, they allow for changes as the scientific progress is made.

And then minority communities have a concern around – a lot of access and affordability concerns but, concerns around, will you – if it turns out that (SENT) is not very feasible and were mostly going to be due, or it just turns out that were mostly going to be doing leftover embryos or egg donations so that for the purposes of – without nucleation, do we need to have sampling from different communities to make sure that if my kid is sick, he or she has just as much chance are your kid even though you're a rich white couple and I'm a poor whatever, of finding a good tissue match in the bank.

So how do we get into the whole question of representation at the level of banking and does that require targeted recruitment, socio, economic and demographic characteristic this is whole good proxies for those kinds of things and if they are, how do we get into the question of recruitment of people from particular population?]

And that brings us again the question of, should you pay, how should you pay, how should you express the risks and benefits to make donation?

Thank you.

Hank Greeley: Thank you. Other comments from the public?

Woman: This is Shannon Smith-Crowley, representing the American College of Obstetricians and Gynecologists.

Hank Greeley: Wait a moment. We need to turn the volume up on here a bit.

Shannon Smith-Crowley: Okay.

Hank Greeley: So, say that again?

Shannon Smith-Crowley: This is Shannon Smith-Crowley, I'm a lobbyist representing the American College of OB-GYNs and the American Society for Reproductive Medicine.

Actually overall we are pretty happy with the serum guidelines. The – representing the Society for Reproductive Medicine, we actually got policies that supports payments to women for the time and trouble of going through the process, you know, the three-four week process, you know, that's not fun.

But we do recognize that under (unintelligible) 71, that that's not possible, so that - at least expenses get reimbursed. But still we've got some guidelines on how if that were to occur, how to basically compensate somebody for what they're going through without providing an undue incentive to have them, you know, I understand some, you know, the folks that are concerned about, women being exploited.

One issue that I did bring up art the serum meeting a couple of weeks ago and we're going to work on some language, is there's fee on -- let me see -- Section 10009 about informed consent.

There – when they talk about the informed consent process and the discussions, it has to occur with the woman – one thing that they have in there that some of us in the reproductive rights community kind of got a little nervous about is they have an adequate period of deliberation for a woman to taking all of the information.

And then the researchers are not supposed to contact her, but she has to re-contact them.

We think women are competent and if there – and this is a long process that they go through with the screening, you know, there's psychological and medical screening and informed consent. This is not a five-minute procedure where they to make up their minds, you know, right then and there.

And then also, because there is kind of this novel – but I – but I think, you know, positive area or where you would test somebody to see if they understood what they were told about the informed consent procedure, that seems to negate a lot of the need for the period of deliberation.

So actually, we're going to go back and work with – the working group, members of CIRM, to see if we can get the spirit in there of making sure that she's got adequate time without giving any ammunition to the folks that want to put in weaning periods for women that are seeking abortions.

Hank Greeley: Okay. Thank you.

Other comments from the public on the telephone line? Other comments in the room? I think I declare the public comments section closed.

We now move to the end of our agenda.

Let me ask Dr. (Ahmad) and his chamber. Did you guys have plans for scheduling the next meeting at this or – I know this is on the agenda, do you think we can actually make progress here or do (unintelligible)?

Man: We can – we have suggestion over here and how much time is needed for the next meeting, what I'm thinking is -- and that's my opinion -- is end of April or early May so that there is in progress through the subcommittees or subgroups during the –those…

Man: Yeah.

Man: …seven, eight weeks.

Man: Yeah.

Hank Greeley: I think May strikes me as possible. May or perhaps, maybe even into early June.

I think end of April might be a little quick.

Man: Okay.

Hank Greeley: But I do suspect that, you know, as you – trying to schedule this first meeting, scheduling this group of people is going to be no picnic. No…

Man: Let me tell you I was lucky to give a four week notice and having all members participating in this, it was a little – on my part, I really want to thank all of you that you came…

Hank Greeley: To committee members May or early June, that sounds reasonable for our next meeting?

Woman: I would say (unintelligible) for those who are academic (unintelligible).

Hank Greeley: Okay.

Man: A little confused as (unintelligible) actually how the progression will work because I suspect it's going to be quite difficult to schedule something over the summer other than various phone interactions and email interactions.

So how many meetings do you imagine there being and sort of what are you trying to get done at the various – how is the work load that you're seeing? If really that means that you're trying to come up with guidelines for public discussions around the end of the summer and you're going to first sort of identify the areas by May, maybe June and it takes that long to get to identify basically what we're going to talk about, my suspicion is that we won't get very far and actually doing much more than the guideline.

(Unintelligible).

Man: It should be more the proportionality of what fraction of the effort of this committee needs – how much effort there is and what fraction is represented by this first little (unintelligible) of effort?

Hank Greeley: I'm an optimistic guy by nature. I actually think we should be able to do our assignment with two more meetings. So that the meeting in May -- hopefully in May, that we could decisions on the ways in which this committee wants to deviate from the CIRM regulations.

And then at – over the summer at some point, that would be written in language that could then be approved or modified at a last meeting, at the end of the summer, the beginning of the fall.

So I see it as two more steps, the working groups, the subcommittees will set up for us for our next meeting, (unintelligible) of issues on which we may or may not choose to deviate from CIRM.

Then there's a writing period and last approval chance, sometime in the late summer, early fall. That's my sense of how this may well proceed, (Greg).

So it looks like we're going to put the onus on you guys of trying to schedule us sometime in May.

Dr. Lubis?

Bertram H. Lubin: We have a copy of the (unintelligible) on that?

Man: Right. There will be (unintelligible) also (unintelligible).

((Crosstalk))

Man: We have that actually transferred?

Man: Right.

Hank Greeley: Okay.

So if I could (unintelligible) just a couple more things and then (unintelligible) the Chair would gladly entertain two motions.

The first motion the Chair would very much like to entertain is a motion thanking the Children's Hospital of Oakland Research Institute, its Director and staff for their hospitality and their beautiful facility.

Okay.

Man: (Unintelligible).

Hank Greeley: Say and I hear a second. All in favor say aye.

Woman: Aye.

Man: Aye.

Woman: Aye.

Man: Aye.

Woman: Aye.

Hank Greeley: All opposed, never talk to me again.

Then the last motion the chair would entertain at this point is a motion to adjourn.

Is there such a motion?

((Crosstalk))

Hank Greeley: Someone has to make (unintelligible).

Woman: I'll move.

Hank Greeley: So move, this is second.

All in favor please signify by standing up and leaving.

Thank you all very much for coming to this meeting. We appreciate it very much.

END